

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

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

k141144

**B. Purpose for Submission:**

Expanded indications for exclusion of pulmonary embolism (PE) to previously cleared D-dimer assay (k964728)

**C. Measurand:**

D-dimer

**D. Type of Test:**

Quantitative immuno-turbidimetric method

**E. Applicant:**

Diagnostica Stago

**F. Proprietary and Established Names:**

STA<sup>®</sup> - Liatest<sup>®</sup> D-Di

**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 Spilt Products, Antigen, Antiserum, Control

4. Panel:

81 Hematology

## H. Intended Use:

1. Intended use(s):

The STA® - Liatest® D-Di kit is an immuno-turbidimetric assay for the quantitative determination of D-dimer in venous plasma (in 3.2% sodium citrate) for use on STA-R®, STA Compact® and STA Satellite® analyzers by professional laboratory personnel. The STA® - Liatest® D-Di is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude pulmonary embolism (PE) and as an aid in the diagnosis of deep venous thrombosis (DVT) in outpatients suspected of PE or DVT.

2. Indication(s) for use:

Same as intended use

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

STA-R® (k983460)  
STA Compact® (k961579)  
STA Satellite® (k082248)

## I. Device Description:

The STA® - Liatest® D-Di assay is a quantitative test for the turbidimetric immuno-assay determination of fibrin degradation products in citrated plasma. The STA® - Liatest® D-Di test kits contain two liquid reagents:

- 6 x 5-ml vials of ready-for-use Tris buffer
- 6 x 6-ml vials of a suspension of microlatex particles coated with two different mouse monoclonal anti-human D-dimer antibodies (8D2 and 2.1.16) stabilized with bovine albumin.

## J. Substantial Equivalence Information:

1. Predicate device name(s):

Diagnostica, Stago STA® - Liatest®  
bioMérieux, VIDAS® D-Dimer Exclusion™

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

k964728  
k040882

3. Comparison with predicate:

- Diagnostica Stago STA<sup>®</sup> - Liatest<sup>®</sup> D-Di

<b>Similarities</b>		
<b>Item</b>	<b>Device STA<sup>®</sup> - Liatest<sup>®</sup> D-Di</b>	<b>Predicate, k964728 STA<sup>®</sup> - Liatest<sup>®</sup> D-Di</b>
Analyte	D-dimer	D-dimer
Assay method	Immuno-turbidimetric method	Immuno-turbidimetric method
Cut-off	0.5 µg/mL (FEU)	0.5 µg/mL (FEU)
Test principle	Immuno-turbidimetric method based on the measurement of light absorbance (at 540 nm) produced by a suspension of microlatex particles coated with specific mouse anti-human D-dimer monoclonal antibodies.	Immuno-turbidimetric method based on the measurement of light absorbance (at 540 nm) produced by a suspension of microlatex particles coated with specific mouse anti-human D-dimer monoclonal antibodies.
Analyzers	IVD analyzers of the STA <sup>®</sup> line: STA-R <sup>®</sup> k983460, STA Compact <sup>®</sup> k961579, and STA Satellite <sup>®</sup> k082248.	IVD analyzers of the STA <sup>®</sup> line: STA-R <sup>®</sup> k983460, STA Compact <sup>®</sup> k961579, and STA Satellite <sup>®</sup> k082248.

<b>Differences</b>		
<b>Item</b>	<b>Device STA<sup>®</sup> - Liatest<sup>®</sup> D-Di</b>	<b>Predicate, k964728 STA<sup>®</sup> - Liatest<sup>®</sup> D-Di</b>
Indication for Use	Indications for Use The STA <sup>®</sup> - Liatest <sup>®</sup> D-Di kit is an immuno-turbidimetric assay for the quantitative determination of D-dimer in venous plasma (in 3.2% sodium citrate) for use on STA-R <sup>®</sup> , STA Compact <sup>®</sup> and STA Satellite <sup>®</sup> analyzers by professional laboratory personnel. The STA <sup>®</sup> - Liatest <sup>®</sup> D-Di is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude pulmonary embolism (PE) and as an aid in the diagnosis of deep venous thrombosis (DVT) in outpatients suspected of PE or DVT.	Quantitative determination of D-dimer in plasma. The assay can be used to aid in the diagnosis of deep venous thrombosis and pulmonary embolism disease.

- bioMérieux VIDAS<sup>®</sup> D-Dimer Exclusion<sup>™</sup>

<b>Similarities</b>		
<b>Item</b>	<b>Device STA<sup>®</sup> - Liatest<sup>®</sup> D-Di</b>	<b>Predicate, k040882 VIDAS<sup>®</sup> D-Dimer Exclusion<sup>™</sup></b>
Indication for use	Quantitative determination of D-dimer in venous plasma (in 3.2% sodium citrate). The assay is intended for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude pulmonary embolism (PE) and as an aid in the diagnosis of deep venous thrombosis (DVT) in outpatients suspected of PE or DVT.	Automated quantitative test for use on the VIDAS instruments for the immunoenzymatic determination of fibrin degradation products (FbDP) in human plasma (sodium citrate) using ELFA technique (Enzyme Linked Fluorescent Assay). The assay is indicated for use in conjunction with a clinical pretest probability assessment model to exclude deep vein thrombosis (DVT) and pulmonary embolism (PE) disease in outpatients suspected of PE or DVT.
Analyte	D-dimer	D-dimer
Cut-off	0.5 µg/mL (FEU)	500 ng/mL (FEU)
Test principle	Immuno-turbidimetric method based on the measurement of light absorbance (at 540 nm) produced by a suspension of microlatex particles coated with specific mouse anti-human D-dimer monoclonal antibodies.	ELFA technique (Enzyme Linked Fluorescent Assay)
Analyzers	IVD analyzers of the STA <sup>®</sup> line.	VIDAS instrument.

<b>Differences</b>		
<b>Item</b>	<b>Device STA<sup>®</sup> - Liatest<sup>®</sup> D-Di</b>	<b>Predicate, k040882 VIDAS<sup>®</sup> D-Dimer Exclusion<sup>™</sup></b>
Assay method	Immuno-turbidimetric method	ELFA technique (Enzyme Linked Fluorescent Assay)
Test principle	Immuno-turbidimetric method based on the measurement of light absorbance (at 540 nm) produced by a suspension of microlatex particles coated with specific mouse anti-human D-dimer monoclonal antibodies.	The assay combines a two-step enzyme immunoassay sandwich method with a final fluorescent detection step (ELFA).

Differences		
Item	Device STA <sup>®</sup> - Liatest <sup>®</sup> D-Di	Predicate, k040882 VIDAS <sup>®</sup> D-Dimer Exclusion <sup>™</sup>
Analyzers	IVD analyzers of the STA <sup>®</sup> line: STA-R <sup>®</sup> , STA Compact <sup>®</sup> , and STA Satellite <sup>®</sup> .	VIDAS instrument

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

CLSI H59-A Quantitative D-dimer for the exclusion of venous thromboembolic disease;  
Approved Guideline

**L. Test Principle:**

The assay is based on the change in turbidity of a microparticle suspension that is measured by photometry. A suspension of latex microparticles, coated by covalent bonding with monoclonal antibodies specific for D-dimer is mixed with the test plasma for which the D-dimer level is to be assayed. An antigen-antibody reaction takes place, leading to an agglutination of the latex microparticles which causes an increase in turbidity of the reaction medium. This increase in turbidity is reflected by an increase in absorbance, the latter being measured photometrically. The increase in absorbance is a function of the D-dimer level present in the test sample. D-dimer levels are expressed in fibrinogen equivalent units (FEU).

**M. Performance Characteristics:**

1. Analytical performance:
  - a. *Precision/Reproducibility:*  
Refer to 510(k) cleared device - k964728
  - b. *Linearity/assay reportable range:*  
Refer to 510(k) cleared device - k964728
  - c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*  
Refer to 510(k) cleared device - k964728
  - d. *Detection limit:*  
Refer to 510(k) cleared device - k964728
  - e. *Analytical specificity:*  
Refer to 510(k) cleared device - k964728
  - f. *Assay cut-off:*  
Refer to 510(k) cleared device - k964728
2. Comparison studies:
  - a. *Method comparison with predicate device:*

Not applicable. Clinical study performed to determine exclusion of pulmonary embolism (PE).

*b. Matrix comparison:*

Refer to 510(k) cleared device - k964728

3. Clinical studies:

*a. Clinical Sensitivity:*

- i. Prospective study: A clinical multi-center study (9 sites over North America and Europe) was performed to demonstrate the ability of STA<sup>®</sup> - Liatest<sup>®</sup> D-Di to exclude pulmonary embolism (PE) using samples of outpatients enrolled in emergency departments prospectively and consecutively. All patients suspected of having a PE were evaluated with the Wells' model to assess their pre-test probability (PTP) score: low, moderate, or high.

Patients with a low or moderate PTP score were considered for D-dimer testing. Those with a positive D-dimer result were referred to imaging studies. Those with negative a D-dimer result were considered as not having PE and assigned to a three-month follow up to evaluate a potential development of PE and were included for analysis. Patients with high PTP were sent for imaging studies and not included in the study population.

The prospective study population was enriched with US banked frozen samples collected from a similar PE clinical study.

Sensitivity, specificity and negative predictive value (NPV) with upper and lower limit of 95 % confidence intervals (CI) were calculated with the STA<sup>®</sup> - Liatest<sup>®</sup> D-Di using the previously cleared clinical cut-off of 0.50 µg/mL (FEU) in the (low and moderate) PTP group of patients:

- US sites: A total of 358 samples of patients from two US clinical centers were used for analysis.

US Prospective		Reference (Imaging or 3-month follow-up)		
		Positive	Negative	Total
D-Dimer	Positive	8	78	86
	Negative	1	271	272
	Total	9	349	358

Sensitivity = 88.9%      95% CI: 51.8% to 99.7%  
 Specificity = 77.7%      95% CI: 72.9% to 81.9%  
 NPV = 99.6%      95% CI: 98.0% to 100.0%  
 PPV = 9.3%      95% CI: 4.1% to 17.5%

- Out of US (OUS) sites: A total of 702 samples of patients from seven OUS

clinical centers were used for analysis.

OUS Prospective		Reference (Imaging or 3-month follow-up)		
		Positive	Negative	Total
D-Dimer	Positive	74	145	219
	Negative	1	482	483
	Total	75	627	702

Sensitivity = 98.7%      95% CI: 92.8% to 100.0%  
 Specificity = 76.9%      95% CI: 73.4% to 80.1%  
 NPV = 99.8%              95% CI: 98.9% to 100.0%  
 PPV = 33.8%              95% CI: 27.6% to 40.5%

- ii. US banked samples: Data from banked samples were obtained from a plasma bank in a similar previous prospective clinical PE study in four US sites. STA<sup>®</sup> - Liatest<sup>®</sup> D-Di was performed on frozen plasma samples from patients diagnosed with PE. Sample stability was assessed by comparison with results obtained prior to freezing (fresh specimens). The results of the stability study were found to be acceptable. Data from the stability study was used to enrich data of the prospective study with positive and negative cases. A total of 70 samples were used for analysis.

US Banked Samples		Reference (Imaging or 3-month follow-up)		
		Positive	Negative	Total
D-Dimer	Positive	16	29	45
	Negative	1	24	25
	Total	17	53	70

Sensitivity = 94.1%      95% CI: 71.3% to 99.9%  
 Specificity = 45.3%      95% CI: 31.6% to 59.6%

- iii. Overall study population: A total of 1,130 samples of patients with a low or moderate PTP were used for final analysis; 1060 samples were from prospective study population and 70 samples were from the US banked frozen samples. The overall prevalence of PE (low and moderate PTP patients) in the prospective study population was 8.4% with 2.7% in the US population and 11.4% in the OUS population.

Demographics:

- Ethnicity: Caucasian 81%, black 13.1%, other 5.9%
- Age: 22-62 years of age
- Gender: 44.4% male, 55.4% female

Overall Study		Reference (Imaging or 3-month follow-up)		
		Positive	Negative	Total
D-Dimer	Positive	98	252	350
	Negative	3	777	780
	Total	101	1029	1130

Sensitivity = 97.0%	95% CI: 91.6% to 99.40%
Specificity = 75.5%	95% CI: 72.8% to 78.1%
NPV = 99.7%	95% CI: 99.2% to 100.0%
PPV = 25.5%	95% CI: 23.5% to 27.7%

*b. Clinical specificity:*

See 3.a. above for clinical specificity results.

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

4. Clinical cut-off:

STA® Liatest® D-Di cut-off is 0.50 µg/mL (FEU); this cut-off was previously established and evaluated in the clearance for k964728.

- Negative if sample level is < 0.50 µg/mL (FEU)
- Positive if sample level is ≥ to 0.50 µg/mL (FEU)

5. Expected values/Reference range:

Same as clinical cut-off 0.50 µg/mL (FEU)

**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.