

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

A. 510(k) Number:

K040882

B. Purpose for Submission:

The purpose of this submission is to obtain clearance for a modification to the indications for use of this device to include an exclusionary claim for pulmonary embolism.

C. Analyte:

D-dimer

D. Type of Test:

ELISA

E. Applicant:

bioMerieux

F. Proprietary and Established Names:

VIDAS® D-dimer Exclusion Assay

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7320

2. Classification:

II

3. Product Code:

DAP

4. Panel:

81 Hematology

H. Intended Use:

1. Intended use(s):

The VIDAS® D-dimer Exclusion Assay is an automated quantitative test for the immunoenzymatic determination of fibrin degradation products (FbDP) in citrated human plasma using the ELFA (Enzyme Linked Fluorescent Assay).

2. Indication(s) for use:

The VIDAS® D-dimer Exclusion Assay is indicated for use in conjunction with a clinical Pre-test Probability Assessment (PTP) assessment model to exclude deep venous thrombosis (DVT) and pulmonary embolism (PE) in outpatients suspected of DVT or PE.

3. Special condition for use statement(s):

4. Special instrument Requirements:

VIDAS analyzers

I. Device Description:

The VIDAS® D-dimer Exclusion Assay is a quantitative for the immunoenzymatic determination of fibrin degradation products in human citrated plasma using the

ELFA technique. The assay is intended for use either on the VIDAS (K981385), or the miniVIDAS (K923579).

Each assay kit contains 60 tests, and consists of the following;

DD2 Reagent Strips- ready to use, polypropylene strip of 10 wells covered with a labeled foil seal. The first well is intended for the sample, and the last well is a cuvette in which the fluorometric reading is performed. The wells in between contain the various reagents required for the assay.

DD2 Solid Phase Receptors (SPR) - The SPR is coated during production with anti-D-Dimer mouse monoclonal immunoglobulin.

C1 and C2 controls – bilevel lyophilized FbDP controls obtained from human plasma.

S1 and S2 calibrators – bilevel lyophilized FbDP calibrators

Master Lot Entry (MLE) Card-the MLE is printed with bar code readable data needed for establishing the Master Curve for that assay.

J. Substantial Equivalence Information:

1. Predicate device name(s):
bioMerieux VIDAS D-Dimer (DD) New Assay-Exclusion DVT Claim
2. Predicate K number(s):
K030328
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative determination of FbDP in citrated human plasma	Same
Methodology	Enzyme Linked Fluorescent Assay (ELFA)	Same
Differences		
Item	Device	Predicate
Indications for use	Along with a Pre-Test Probability Assessment Model (PTP), for the exclusion of DVT and PE	Along with a PTP for the exclusion on DVT

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

L. Test Principle:

The assay combines a two-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA).

All of the assay steps are performed automatically by the instrument. The sample is transferred into the well of the SPR containing an alkaline-phosphatase labeled anti-FbDP monoclonal antibody. The sample /conjugate mixture is cycled in and out of the SPR several times to increase the reaction speed. The antigen in the sample binds to the antibodies coated on the SPR and to the conjugate.

The remaining free antigen sites are then saturated by cycling the conjugate in the fifth well of the reagent strip in and out of the SPR. Unbound components are eliminated during the washing steps.

Substrate is then cycled in and out of the SP. The conjugate catalyzes the hydrolysis of the substrate into a fluorescent product that is measured at 450 nm. The intensity of the fluorescence is proportional to the concentration of antigen and present in the sample. Results are calculated in relation to two calibration curves stored in memory.

M. Performance Characteristics (if/when applicable):1. Analytical performance:*a. Precision/Reproducibility:*

			Within-run reproducibility	Reproducibility
Plasma	N	Concentration (ng/ml) (FEU)	%CV	%CV
Level 1	80	264	5.0	5.7
Level 2	80	549	3.9	5.8
Level 3	80	7283	5.3	7.1

b. Linearity/assay reportable range:

45 to 10,000 ng/ml (FEU)

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

The smallest concentration of D-Dimer significantly different from the zero concentration with a risk α of 5%: ≤ 45 ng/ml (FEU)

e. Analytical specificity:

Fibrinogen: the results of the dilution tests for two plasmas with titers of 2076 ng/ml (FEU) and 8093 ng/ml (FEU) are not significantly different when the kit diluent for plasma with a low concentration of D-Dimer is used.

Fibrinogen degradation products: the excess concentration of plasma with a titer of 63 ng/ml (FEU) of D-Dimer, with a mixture of fibrinogen degradation products, does not modify the result up to a concentration ratio of 1 to 100.

The specificity of the two antibodies used in this assay was not tested against FDPE, therefore cross-reactivity cannot be ruled out.

f. Assay cut-off:
500 ng/ml (FEU)

2. Comparison studies:

a. Method comparison with predicate device:

b. Matrix comparison:

3. Clinical studies:

a. Clinical sensitivity:

DVT EXCLUSION

Frozen samples collected from patients enrolled in a multi-center prospective cohort study were used. Consecutive eligible outpatients (n= 556) with a first suspected DVT from 3 sites were evaluated. Patients were classified as having a high, moderate, or low pretest probability of DVT, using the Wells model to estimate probability. A d-dimer result ≥ 500 ng FEU/ml was considered positive and a result of < 500 ng FEU/ml was considered negative. Those patients having a negative D-dimer result and a low or moderate PTP underwent no further diagnostic testing, and were followed for 3 months for development of DVT. Patients with a positive d-dimer test result and/or high PTP underwent serial compression ultrasound.

Total Population

Patients With Suspected DVT	N	%Sensitivity (95% CI)	% Specificity (95% CI)	% Negative Predictive Value (95%) CI
All probabilities	555	100.0 (93.6-100.0)	32.9 (28.8 – 37.2)	100.0 (97.8-100.0)

Patients with low PTP

Patients With Suspected DVT	N	%Sensitivity (95% CI)	% Specificity (95% CI)	% Negative Predictive Value (95%) CI
Low probability	295	100.0 (81.5-100.0)	39.7 (33.9 – 45.7)	100.0 (96.7-100.0)

Patients with Moderate PTP

Patients With Suspected DVT	N	%Sensitivity (95% CI)	% Specificity (95% CI)	% Negative Predictive Value (95%) CI
Mod probability	189	100.0 (80.5-100.0)	26.7 (20.3 – 34.0)	100.0 (92.3-100.0)

Patients with High PTP

Patients With Suspected DVT	N	%Sensitivity (95% CI)	% Specificity (95% CI)	% Negative Predictive Value (95%) CI
High probability	71	100.0 (83.9-100.0)	16.0 (7.2 – 29.1)	100.0 (63.1-100.0)

PE EXCLUSION

In a multi-center (3) prospective study, fresh samples were collected from patients presenting to the ER with suspected PE (n=965). Patients were classified as having a high, moderate, or low pretest probability of PE, using the WICKIE model to estimate probability. A d-dimer result ≥ 500 ng FEU/ml was considered positive and a result of < 500 ng FEU/ml was considered negative. Those patients having a negative D-dimer result received no treatment, and underwent no further diagnostic testing. Patients with a positive d-dimer test result were further evaluated using ultrasound, Helical CT scans, and/or angiography. These patients were followed up for 3 months to evaluate any possible VTE and episodes of bleeding.

Total Population

All Patients	%Sensitivity (95% CI)	% Specificity (95% CI)	% Negative Predictive Value (95% CI)	%Positive Predictive Value (95% CI)
965	100.0 (98.4-100.0)	37.7 (34.2 – 41.3)	100.0 (98.7-100.0)	32.4 (28.9-36.1)

Patients with low and moderate PTP

Low & Intermediate	%Sensitivity (95% CI)	% Specificity (95% CI)	% Negative Predictive Value (95%) CI	%Positive Predictive Value (95% CI)
891	100% (97.7-100%)	37.6 (34.0-41.2)	100.0 (98.7 – 100.0)	25.8 (22.4-29.5)

Patients with High PTP

High	%Sensitivity (95% CI)	% Specificity (95% CI)	% Negative Predictive Value (95%) CI	%Positive Predictive Value (95% CI)
74	100.0 (94.3-100.0)	45.5 (16.7 – 76.6)	100.0 (47.8-100.0)	91.3 (82.0-96.7)

b. Clinical specificity:

See above

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

4. Clinical cut-off:
500 ng/ml (FEU)
5. Expected values/Reference range:
In a study involving 200 blood donors, 96% of values were below 500 ng/ml (FEU).

N. Conclusion:

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