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

A. 510(k) Number:

K070927

B. Purpose for Submission:

To seek clearance for modification to HemosIL D-Dimer HS

C. Measurand:

D-Dimer

D. Type of Test:

Latex-enhanced immunoturbidmetric assay

E. Applicant:

Instrumentation Laboratory Co.

F. Proprietary and Established Names:

HemosIL D-Dimer HS

G. Regulatory Information:

1. Regulation section:

   864.7320

2. Classification:

   II

3. Product code:

   DAP

4. Panel:

   Hematology

H. Intended Use:

1. Intended use(s):

   HemosIL D-Dimer HS is an automated latex enhanced immunoassay for the quantitative determination of D-Dimer in human citrated plasma on the ACL TOP for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude venous thromboembolism (VTE) in outpatients suspected of deep venous thrombosis (DVT) and pulmonary embolism (PE).

2. Indication(s) for use:

   HemosIL D-Dimer HS is an automated latex enhanced immunoassay for the quantitative determination of D-Dimer in human citrated plasma on the ACL TOP for use in conjunction with a clinical pretest probability (PTP) assessment model to exclude venous thromboembolism (VTE) in outpatients suspected of deep venous thrombosis (DVT) and pulmonary embolism (PE).

3. Special conditions for use statement(s): N/A

4. Special instrument requirements:

   ACL TOP

I. Device Description:

The HemosIL D-Dimer HS test kit consists of latex reagent, reaction buffer, D-Dimer calibrator, and low and high D-Dimer controls. The assay is intended for use on the ACL TOP instrument.

J. Substantial Equivalence Information:

1. Predicate device name(s):

    Biomerieux Vidas D-Dimer Exclusion Assay
    HemosIL D-Dimer HS

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

   K040882
   K050544

3. Comparison with predicate:

Similarities			
Item	**Modified Device: HemosIL D-Dimer HS**	**Predicate Device: HemosIL D-Dimer HS (K050544)**	**Predicate Device: Biomerieux Vidas® D-Dimer Exclusion Assay (K040882)**
Indications for use	For use in conjunction with a clinical pretest probability (PTP) assessment model to exclude venous thromboembolism (VTE) [deep venous thrombosis (DVT) and pulmonary embolism (PE)].		For use in conjunction with a clinical Pre-test Probability (PTP) assessment model to exclude deep venous thrombosis (DVT) and pulmonary embolism (PE) in outpatients suspected of DVT and PE.
Differences			
Item	**Modified Device: HemosIL D-Dimer HS**	**Predicate Device: HemosIL D-Dimer HS (K050544)**	**Predicate Device: Biomerieux Vidas® D-Dimer Exclusion Assay (K040882)**
Assay principle	Same as K050544	Latex-enhanced immunoturbidmetric assay	Two-step enzyme immunoassay sandwich method with a final fluorescent detection
Measuring Range	Same as K050544	150 - 69000 ng/mL with automatic rerun	45 - 10000 ng/mL (FEU)
Detection Limit	Same as K050544	21 ng/mL	45 ng/mL (FEU)
Interferences	Same as K050544	Hemoglobin up to 500 mg/dL Bilirubin up to 18 mg/dL Triglycerides up to 1327 mg/dL FDP up to 10 μg/mL Rheumatoid Factor up to 1400 UI/mL	None of the following factors have been found to significantly influence this assay: hemolysis, lipemia, bilirubinemia, rheumatoid factor. It is recommended not to use samples that appear to be clearly hemolyzed, lipemic, or icteric.
Clinical Cut-off	Same as K050544	230 ng/mL	500 ng/mL (FEU)

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

L. Test Principle:

The assay is based on the decrease of the transmitted light caused by the aggregates which form when a patient plasma containing D-Dimer is mixed with latex particles coated with monoclonal antibody. The degree of agglutination is directly

proportional to the concentration of D-Dimer in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance: extended claim, see original submission (K050544) for analytical studies.

   a. *Precision/Reproducibility:*

   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:*

   HemosIL D-Dimer HS was used in a multi-center management study involving 668 samples from patients admitted consecutively to the emergency unit with suspected DVT or PE. 307 patients were suspected of DVT and 361 patients were suspected of PE.

   The Wells model was used to assess PTP (pre-test probability) score. The patients were classified as having a high, moderate, or low probability of DVT or PE.

   - Patients with a negative D-Dimer test result and a low PTP score underwent no further diagnostic testing and were followed-up after 3 months for development of DVT or PE.
   - For patients with a negative D-Dimer test result and a moderate PTP, it was the physician's decision whether to follow-up after 3 months or to undergo imaging techniques. Data indicated that all patients with a negative D-Dimer test and a moderate PTP received either 3 months of follow-up, or imaging with 3 months of follow-up if the imaging result was negative.
   - Patients with a positive D-Dimer test result or a high PTP score were imaged.
   - As of the 3 month follow-up, none of the patients that were negative through D-Dimer testing had developed DVT or PE.

Previously established clinical cutoff of 230 ng/mL for HemosIL D-Dimer HS (K050544) was used for calculation. Statistical evaluation of the respective data sets from the four sites was performed using analysis of variance (ANOVA) to verify whether the three PE sites could be pooled and the three DVT sites could be pooled. The result was within acceptable limit ($p>0.05$).

- DVT samples: Of the 307 total DVT suspected patients (179 females, 128 males). The overall prevalence of DVT in the total population of samples was 20.2% (62/307).

- PE samples: Of 361 total PE suspected patients (204 females, 157 males). The overall prevalence of PE in the total population of samples was 16.1% (58/361).

The sensitivity, specificity and negative predictive value (NPV) of HemosIL D-Dimer HS for DVT and PE is summarized below with the corresponding 95% confidence intervals (CI):

Combined DVT Performance

DVT Performance	All samples	High PTP	Low + Moderate PTP
N	307	54	253
Sensitivity	100.0% (62/62) (94.2%-100.0%)	100.0% (28/28) (87.7%-100.0%)	100.0% (34/34) (89.7%-100.0%)
Specificity	38.4% (94/245) (32.2%-44.8%)	34.6% (9/26) (17.2%-55.7%)	38.8% (85/219) (32.3%-45.6%)
Negative Predictive value	100.0% (94/94) (96.2%-100.0%)	100.0% (9/9) (66.4%-100.0%)	100.0% (85/85) (95.8%-100.0)
Positive Predictive value	29.1% (62/213) (23.1%-35.7%)	62.2% (28/45) (46.5%-76.2%)	20.2% (34/168) (14.4%-27.1%)
Prevalence	20.2% (62/307) (15.8%-25.1%)	51.9% (28/54) (37.8%-65.7%)	13.4% (34/253) (9.5%-18.3%)

Combined PE Performance

PE Performance	All samples	High PTP	Low + Moderate PTP
n	361	28	333
Sensitivity	100.0% (58/58) (93.8%-100.0%)	100.0% (10/10) (69.2%-100.0%)	100.0% (48/48) (92.6%-100.0%)
Specificity	35.6% (108/303) (30.2%-41.3%)	16.7% (3/18) (3.6%-41.4%)	36.8% (105/285) (31.2%-42.7%)
Negative Predictive value	100.0% (108/108) (96.6%-100.0%)	100.0% (3/3) (29.2%-100.0%)	100.0% (105/105) (96.5%-100.0%)
Positive Predictive value	22.9% (58/253) (17.9%-28.6%)	40.0% (10/25) (21.1%-61.3%)	21.1% (48/228) (15.9%-26.9%)
Prevalence	16.1% (58/361) (12.4%-20.3%)	35.7% (10/28) (18.6%-55.9%)	14.4% (48/333) (10.8%-18.7%)

   b. Matrix comparison:

 3. <u>Clinical studies</u>: N/A

   a. Clinical Sensitivity:

   b. Clinical specificity:

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

 4. <u>Clinical cut-off</u>**:** 230 ng/mL, same as K050544

 5. <u>Expected values/Reference range:</u> N/A

N. Proposed Labeling:

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

O. Conclusion:

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