

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

A. 510(k) Number:

K073042

B. Purpose for Submission:

To seek clearance for modification to the Indications for Use of the HemosIL D-Dimer to include an exclusionary claim for deep venous thromboembolism and pulmonary embolism

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

G. Regulatory Information:

1. Regulation section:

864.7320

2. Classification:

II

3. Product code:

DAP

4. Panel:

81 Hematology

H. Intended Use:

1. Intended use(s):

HemosIL D-Dimer is an automated latex enhanced immunoassay for the quantitative determination of D-Dimer in human citrated plasma on IL Coagulation Systems.

2. Indication(s) for use:

HemosIL D-Dimer is used 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:

IL Coagulation Systems

I. Device Description:

The HemosIL D-Dimer assay is a quantitative test for the turbidimetric immunoassay determination of fibrin degradation products in citrated plasma. The HemosIL D-Dimer test kit consists of latex reagent, reaction buffer, and D-Dimer calibrator. The latex reagent contains latex particles coated with a monoclonal antibody which is highly specific for the D-Dimer domain included in fibrin soluble derivatives.

J. Substantial Equivalence Information:

1. Predicate device name(s):

HemosIL D-Dimer HS

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

K070927

3. Comparison with predicate:

Similarities		
Item	Modified Device: HemosIL D-Dimer	Predicate Device: HemosIL D-Dimer HS (K070927)
Indications for Use	Same as K070927	For use in conjunction with a clinical pretest probability (PTP) assessment model to exclude venous thromboembolism (VTE) in outpatients suspected of deep venous thromboembolism (DVT) and pulmonary embolism (PE).
Assay principle	Same as K070927	Latex-enhanced immunoturbidimetric assay
Sample	Same as K070927	Citrated plasma
Clinical Cut-off	Same as K070927	230 ng/mL
Differences		
Item	Modified Device: HemosIL D-Dimer	Predicate Device: HemosIL D-Dimer HS (K070927)
Instrument	IL Coagulation Systems	ACL TOP only
Measuring Range	200 – 5,250 ng/mL with automatic rerun	150 – 69,000 ng/mL with automatic rerun
Detection Limit	ACL Family: 140 ng/mL ACL Futura/ACL Advance: 156 ng/mL ACL TOP: 69 ng/mL	ACL TOP: 21 ng/mL
Within-run Precision (% CV)	ACL Family: <ul style="list-style-type: none"> 4.5% at 246 ng/mL 6.01% at 310 ng/mL 2.42% at 732 ng/mL ACL Futura/ACL Advance: <ul style="list-style-type: none"> 11.82% at 304 ng/mL 3.59% at 813 ng/mL ACL TOP: <ul style="list-style-type: none"> 6.8% at 282 ng/mL 4.6% at 340 ng/mL 2.5% at 729 ng/mL 	ACL TOP: <ul style="list-style-type: none"> 8.3% at 180 ng/mL 3.7% at 314 ng/mL 2.0% at 677 ng/mL
Interferences	ACL Family, ACL Futura/ACL Advance Systems: <ul style="list-style-type: none"> Hemoglobin up to 50 mg/dL Bilirubin up to 5 mg/dL Lipids up to 1000 mg/dL Rheumatoid Factor up to 60 IU/mL ACL TOP <ul style="list-style-type: none"> Hemoglobin up to 100 mg/dL Bilirubin up to 10 mg/dL Triglycerides up to 1500 mg/dL The presence of Rheumatoid Factor 	ACL TOP: <ul style="list-style-type: none"> Hemoglobin up to 500 mg/dL Bilirubin up to 18 mg/dL Triglycerides up to 1327 mg/dL Rheumatoid Factor up to 1400 UI/mL

	may produce an overestimation of the test result	
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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 (K050278) for analytical studies.

- a. *Precision/Reproducibility:* Additional precision study using a sample close to the cut-off:

Instrument	N	Mean (ng/mL)	CV% (within-run)	CV% (Total)
ACL ELITE PRO	80	246	4.5	11.7
ACL TOP	80	282	6.8	9.0

- 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: extended claim, see original submission (K050278) for comparison studies

- a. *Method comparison with predicate device:*

- b. *Matrix comparison:* N/A

3. Clinical studies:

- a. *Clinical Sensitivity:*

HemosIL D-Dimer was used in a multi-center management study involving samples from patients admitted consecutively to the emergency unit with

suspected DVT or PE using representative IL Coagulation Systems: ACL TOP and ACL ELITE instruments. The ACL TOP represents the linear analyzer group (ACL TOP, ACL Advance/Futura), the ACL ELITE represents the centrifugal group (ACL 8/9/10000/Elite/ElitePro, ACL 100-7000 Series).

The Wells model was used to assess PTP (pre-test probability) score. The patients were classified as having a low, moderate, or high 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. Data indicated that all patients received 3 months of follow-up if the imaging result was negative.
- As of the 3 month follow-up, none of the patients that were negative through D-Dimer testing and imaging had developed DVT or PE.
- Through imaging techniques, one patient with a negative D-Dimer test result on the ACL ELITE and a moderate PTP score was confirmed for PE.

Previously established clinical cut-off of 230 ng/mL for HemosIL D-Dimer (K050278) 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 results were within acceptable limit ($p > 0.05$).

ACL TOP: 302 patients were suspected of DVT and 330 patients were suspected of PE.

- DVT samples: Of the 302 total DVT suspected patients (175 females, 127 males). The overall prevalence of DVT in the total population of samples was 19.5% (59/302).
- PE samples: Of 330 total PE suspected patients (188 females, 142 males). The overall prevalence of PE in the total population of samples was 15.2% (50/330).

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

ACL TOP			
DVT Performance	All samples	High PTP	Low + Moderate PTP
N	302	53	249
Sensitivity	100.0% (59/59) (93.9%-100.0%)	100.0% (27/27) (87.2%-100.0%)	100.0% (32/32) (89.1%-100.0%)
Specificity	41.6% (101/243) (35.3%-48.0%)	34.6% (9/26) (17.2%-55.7%)	42.4% (92/217) (35.7%-49.3%)
Negative Predictive Value	100.0% (101/101) (96.4%-100.0%)	100.0% (9/9) (66.4%-100.0%)	100.0% (92/92) (96.1%-100.0%)
Positive Predictive Value	29.4% (59/201) (23.2%-36.2%)	61.4% (27/44) (45.5%-75.6%)	20.4% (32/157) (14.4%-27.5%)
Prevalence	19.5% (59/302) (15.2%-24.5%)	50.9% (27/53) (36.8%-64.9%)	12.9% (32/249) (9.0%-17.7%)
PE Performance	All samples	High PTP	Low + Moderate PTP
N	330	24	306
Sensitivity	100.0% (50/50) (92.9%-100.0%)	100.0% (7/7) (59.0%-100.0%)	100.0% (43/43) (91.8%-100.0%)
Specificity	29.3% (82/280) (24.0%-35.0%)	17.6% (3/17) (3.8%-43.4%)	30.0% (79/263) (24.6%-36.0%)
Negative Predictive Value	100.0% (82/82) (95.6%-100.0%)	100.0% (3/3) (29.2%-100.0%)	100.0% (79/79) (95.4%-100.0%)
Positive Predictive Value	20.2% (50/248) (15.4%-25.7%)	33.3% (7/21) (14.6%-57.0%)	18.9% (43/227) (14.1%-24.7%)
Prevalence	15.2% (50/330) (11.5%-19.5%)	29.2% (7/24) (12.6%-51.1%)	14.1% (43/306) (10.4%-18.5%)

ACL ELITE: 298 patients were suspected of DVT and 331 patients were suspected of PE.

- DVT samples: Of the 298 total DVT suspected patients (173 females, 125 males). The overall prevalence of DVT in the total population of samples was 20.5% (61/298).
- PE samples: Of 331 total PE suspected patients (193 females, 138 males). The overall prevalence of PE in the total population of samples was 15.1% (50/331).

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

ACL ELITE			
DVT Performance	All samples	High PTP	Low + Moderate PTP
N	298	54	244
Sensitivity	100.0% (61/61) (94.1%-100.0%)	100.0% (29/29) (88.1%-100.0%)	100.0% (32/32) (89.1%-100.0%)
Specificity	33.8% (80/237) (27.8%-40.2%)	24.0% (6/25) (9.4%-45.1%)	34.9% (74/212) (28.5%-41.7%)
Negative Predictive Value	100.0% (80/80) (95.5%-100.0%)	100.0% (6/6) (54.1%-100.0%)	100.0% (74/74) (95.1%-100.0%)
Positive Predictive Value	28.0% (61/218) (22.1%-34.4%)	60.4% (29/48) (45.3%-74.2%)	18.8% (32/170) (13.2%-25.5%)
Prevalence	20.5% (61/298) (16.0%-25.5%)	53.7% (29/54) (39.6%-67.4%)	13.1% (32/244) (9.1%-18.0%)
PE Performance	All samples	High PTP	Low + Moderate PTP
N	331	25	306
Sensitivity	98.0% (49/50) (89.4%-99.9%)	100.0% (8/8) (63.1%-100.0%)	97.6% (41/42) (87.4%-99.9%)
Specificity	41.3% (116/281) (35.5%-47.3%)	41.2% (7/17) (18.4%-67.1%)	41.3% (109/264) (35.3%-47.5%)
Negative Predictive Value	99.1% (116/117) (95.3%-100.0%)	100.0% (7/7) (59.0%-100.0%)	99.1% (109/110) (95.0%-100.0%)
Positive Predictive Value	22.9% (49/214) (17.4%-29.1%)	44.4% (8/18) (21.5%-69.2%)	20.9% (41/196) (15.4%-27.3%)
Prevalence	15.1% (50/331) (11.4%-19.4%)	32.0% (8/25) (14.9%-53.5%)	13.7% (42/306) (10.1%-18.1%)

b. Clinical specificity: see above

4. Clinical cut-off: 230 ng/mL; same as K050278

5. Expected values/Reference range: 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.