

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

A. 510(k) Number:

k133582

B. Purpose for Submission:

To obtain clearance of a modified assayed control materials intended for the quality control of the HemosIL D-Dimer HS 500 assay as performed on the ACL TOP Family Systems.

C. Measurand:

D-dimer fragment of fibrin

D. Type of Test:

Latex based immunoturbidimetric assay

E. Applicant:

Instrumentation Laboratory, Inc.

F. Proprietary and Established Names:

HemosIL D-Dimer HS 500 Controls

G. Regulatory Information:

1. Regulation section:

CFR §864.5425 Multipurpose system for in vitro coagulation studies

2. Classification:

Class II

3. Product code:

GGN, Plasma, Coagulation Control

4. Panel:

Hematology (81)

H. Intended Use:

1. Intended use(s):

D-Dimer HS 500 Controls are assayed human-sourced controls intended for the quality control of the HemosIL D-Dimer HS 500 assay as performed on the ACL TOP Family

Systems, in a clinical laboratory setting. The controls are intended for in vitro diagnostic use.

Level 1 D-Dimer HS 500 Control is intended for the assessment of precision and accuracy of the assay around the clinical cut-off for VTE (500ng/mL FEU).

Level 2 D-Dimer HS 500 Control is intended for the assessment of precision and accuracy of the assay at abnormal D-Dimer levels (above the cut-off).

2. Indication(s) for use:

Same as intended use.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

ACL TOP family of analyzers (k073377).

I. Device Description:

The Level 1 and Level 2 D-Dimer HS 500 Controls are prepared by means of a dedicated process and contain different concentrations of partially purified D-Dimer obtained by digestion of Factor XIIIa cross-linked human fibrin with human plasmin.

The HemosIL D-Dimer HS 500 Controls kit consists of 2 liquid control levels: Level 1 (Cat. No.0020013110) and Level 2 (Cat. No.0020013120). Each control consists of 5 vials x1 mL of a liquid solution of D-Dimer partially purified from human fibrin digested with human plasmin containing bovine serum albumin, buffer, stabilizers and preservative. Use of both controls is recommended for a complete quality control program.

The kit is only available in one (1) configuration (Cat No. 0020013100).

J. Substantial Equivalence Information:

1. Predicate device name(s) and Predicate 510(k) number(s):

HemosIL D-Dimer HS 500 Controls, Low Control (k090264)
HemosIL D-Dimer HS 500 Controls, High Control (k090264)

2. Comparison with predicate:

Similarities		
Item	Device HemosIL D-Dimer HS 500 Controls	Predicate HemosIL D-Dimer HS 500 Controls
Intended Use/ Indications for Use	HemosIL D-Dimer HS 500 Controls are assayed, human-sourced controls intended for the quality control of the HemosIL D-Dimer HS 500 assay as performed on the ACL TOP Family Systems, in a clinical laboratory setting. The controls are intended for in vitro diagnostic use. Level 1 D-D HS 500 Control is intended for the assessment of precision and accuracy of the assay around the clinical cut-off for VTE (500 ng/mL FEU). Level 2 D-D HS 500 Control is intended for the assessment of precision and accuracy of the assay at abnormal D-Dimer levels (above the cut-off).	For the quality control of the D-Dimer HS 500 assay performed on the ACL TOP Family Systems
Principle of Operation	Latex-based immunoturbidimetric immunoassay	Same
Technology	The Controls are prepared by means of a dedicated process and contain different concentrations of partially purified D-Dimer obtained by digestion of Factor XIIIa cross-linked human fibrin with human plasmin.	Same
Opened Stability (@ 2-8°C)	1 month	Same

Differences		
Item	Device HemosIL D-Dimer HS 500 Controls	Predicate HemosIL D-Dimer HS 500 Controls
Kit Part #	0020013100	0020500200
Delivery	Liquid	Lyophilized
Composition	Level 1 D-D HS 500 Control 5 vials x 1 mL of a liquid solution of D-Dimer partially purified from human fibrin digested with human plasmin and stabilized with a crosslinker containing bovine serum albumin, buffer, stabilizers and preservative	Low D-D HS 500 Control 5 vials x 1 mL of a lyophilized solution of D-Dimer partially purified from human fibrin digested with human plasmin containing bovine serum albumin, buffer, stabilizers and preservative.

Differences		
Item	Device HemosIL D-Dimer HS 500 Controls	Predicate HemosIL D-Dimer HS 500 Controls
	Level 2 D-D HS 500 Control 5 vials x 1 mL of a liquid solution of D-Dimer partially purified from human fibrin digested with human plasmin and stabilized with a crosslinker containing bovine serum albumin, buffer, stabilizers and preservative.	High D-D HS 500 Control 5 vials x 1 mL of a lyophilized solution of D-Dimer partially purified from human fibrin digested with human plasmin containing bovine serum albumin, buffer, stabilizers and preservative.
	Buffer Hepes (50 mM), NaCl (100 mM), CaCl ₂ (2 mM), NaN ₃ (1g/L), BSA (10g/L) at a pH of 7.5	Buffer Hepes (50 mM), NaCl (100 mM), Glycine 4%, NaN ₃ (1g/L), BSA (10g/L) at a pH of 7.5
On Board Stability (ACL TOP 15-25°C)	24 hours	8 hours
Stability @ - 20°C	3 months	2 months

K. Standard/Guidance Document Referenced:

- CLSI EP05-A2
- CLSI EP15-A2
- CLSI EP25-A
- CLSI H59-A

L. Test Principle:

The controls are intended for the quality control of the HemosIL D-Dimer HS 500 assay on Instrumentation Laboratory's ACL TOP family analyzers. The controls contain different concentrations of partially purified D-Dimer obtained by digestion of human fibrin with human plasmin.

In the D-Dimer assay the latex reagent coated with the monoclonal antibody specific for the D-Dimer domain agglutinates upon binding to the antigen present in the patient plasma. The degree of agglutination is directly proportional to the concentration of D-Dimer in the sample and is determined by measuring the decrease of transmitted light caused by the aggregates (turbidimetric immunoassay).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision study:

The Sponsor tested 3 lots of controls using one (1) lot of HemosIL D-Dimer HS 500 assay on a representative member (1) of the ACL TOP Family (ACL TOP 500). Each control was analyzed for 20 days, with 2 runs a day, 2 replicates per run for each sample level (N=80/ per level/ per instrument). Calibration was performed at the start of the study (T=0) with the kit's calibration plasma.

Acceptance criteria were set at $\leq 8\%$ for within-run CV% and $\leq 12\%$ for total CV. This study was considered sufficient to support the precision claim as the %CV for each tested variable meets the pre-specified acceptance criteria. Results are summarized in the table.

Control Level	Level 1	Level 2
Grand Mean (ng/mL FEU)	566	1730
Within Run (%CV)	4.59%	1.80%
Run-to-Run (%CV)	2.4%	0.6%
Day-to-Day (%CV)	1.5%	0.5%
Lot-to-Lot (%CV)	2.3%	1.9%
Total (%CV)	5.86%	2.69%

The variability between instrument platforms ACLTOP 300/500/700 was tested in a separate experiment, using three (3) lots of HemosIL D-Dimer HS Controls by three (3) operators using three (3) instruments and one (1) lot of HemosIL D-Dimer Reagent. In this study, each operator used a different lot of control material and a different instrument type, representing "worst case" scenario. The instrument to instrument variability was less than 10%. The table below shows a summary of the results.

Statistics	Control Level 1	Control Level 2
Overall Mean (ng/mL FEU)	527.77	1842.02
Between Runs (%CV)	3.22%	0.40%
Between Days (%CV)	0.00%	0.00%
Between (Control Lot + Instruments)	2.13%	9.47%
Repeatability (%CV)	5.83%	1.99%
Total (%CV)	6.99%	9.69%
Between Instruments Specification	$\leq 10\%$	$\leq 10\%$
PASS/FAIL	PASS	PASS

Reproducibility study

A reproducibility study was performed in three (3) different locations using one (1) lot of HemosIL D-Dimer HS 500 controls (PN 0020013100) and one (1) lot of HemosIL D-Dimer HS 500 assay on an ACL TOP 700. At each site each control level was analyzed for 20 days, with 2 runs a day, 2 replicates per run for each sample level (N=80/per level/per site). Calibration was performed at the start of the study (T=0) with the kit's calibrator. The results met pre-specified acceptance criteria of

repeatability CV% $\leq 8\%$ and total CV% $\leq 12\%$ for Level 1 Control and $\leq 10\%$ for Level 2 Control. For a summary of the results please see table below.

Control Level	Site 1		Site 2		Site 3	
	Level 1	Level 2	Level 1	Level 2	Level 1	Level 2
Mean (ng/mL FEU)	483.84	1648.69	520.91	1647.38	537.15	1750.15
Repeatability (CV %)	2.15%	1.49%	3.81%	1.50%	3.10%	1.25%
Repeatability Spec.	$\leq 8\%$					
Repeatability	PASS	PASS	PASS	PASS	PASS	PASS
Between run (CV%)	0.79%	0.29%	1.42%	0.17%	0.51%	0.90%
Between day (CV%)	0.61%	0.89%	0.79%	0.72%	1.58%	0.83%
Total (CV%)	2.37%	1.76%	4.14%	1.67%	3.52%	1.75%

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Value Assignment

A value assignment study is performed 4 times on a minimum of two (2) ACL TOP units. For each time, the assay is calibrated using the Reagent House Standard and the Calibrator House Standard followed by analyzing 8 samples of the Control Test and 8 of the Control House Standard. In total 32 results are obtained for each material.

The package insert acceptance range is $\pm 18\%$ of the target value for Level 1 and $\pm 10\%$ of the target value for Level 2 controls. Once produced, acceptance ranges for a specific lot are printed on the package insert sheet, i.e. every lot has individualized target value. The customer acceptance criteria are then $\pm 20\%$ of the target values for Level 1 and $\pm 20\%$ for Level 2 control.

Stability

Real-time shelf life stability studies are ongoing. The study will be completed on an ACL TOP 700 analyzer using three (3) lots of controls and three (3) lots of the assay reagent. The three lots of assay reagent are to be used instead of one lot due to shorter stability of the assay reagent as compare to stability of controls.

For on-board stability and in open-vial stability studies, two (2) lots of controls were tested using one (1) lot of the reagent. The stability claims were calculated using an acceptance range of $\pm 15\%$ compared to the unstressed baseline or compared against initial values (T=0) when placed on-board the instrument. The results support open vial stability for 1 month when open vial is re-stored at 2-8°C and 3 months when open vial is re-stored at -20°C. Also, provided data support 24 hour on-board stability at 15-25°C.

d. Detection limit:

Not applicable

e. Analytical specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

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

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Reference ranges are on each package insert based on each lot of control Value assignment

N. Proposed Labeling:

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

O. Conclusion:

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