510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K163498

B. Purpose for Submission:

Clearance of a new device

C. Measurand:

Heparin anti-Xa

D. Type of Test:

Quantitative

E. Applicant:

Maine Standards Company LLC

F. Proprietary and Established Names:

VALIDATE® Heparin Calibration Verification/Linearity Test Kit

G. Regulatory Information:

1. Regulation section:

   21 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:

   Same as indications for use below.

2. Indication for use:

   VALIDATE® Heparin Calibration Verification/Linearity Test Kit solutions are assayed quality control materials intended for *in vitro* diagnostic use in the quantitative determination of linearity, calibration verification and verification of reportable range for Heparin Anti-Xa activity on automated instruments in a clinical laboratory setting by laboratory personnel. The product is intended for use on the IL ACL TOP 500® analyzer.

3. Special conditions for use statement:

   For prescription use only

4. Special instrument requirements:

   Instrumentation Laboratory (IL) ACL TOP® 500 (K160276)

I. Device Description:

The VALIDATE® Heparin Calibration Verification/Linearity Kit consists of five liquid levels containing heparin in a human plasma base matrix. Each level contains 3.0 mL.

J. Substantial Equivalence Information:

1. Predicate device name:

   HemosIL UF Heparin Controls
   HemosIL LMW Heparin Controls

2. Predicate 510(k) number:

   K090209

3. Comparison with predicate:

Similarities		
Item	Device VALIDATE® Heparin Calibration Verification/Linearity Test Kit	Predicates HemosIL LMW Controls HemosIL UF Heparin Controls
Intended Use	VALIDATE® Heparin Calibration Verification/Linearity Test Kit solutions are assayed quality control materials intended for *in vitro* diagnostic use in the quantitative determination of linearity, calibration verification and verification of reportable range for Heparin Anti-Xa activity on automated instruments in a clinical laboratory setting by laboratory personnel. The product is intended for use on the IL ACL TOP 500® analyzer.	HemosIL LMW Heparin Controls (Assayed): For the quality control of the HemosIL Liquid Heparin assay when testing for low molecular weight heparin (LMW) on IL Coagulation Systems, (ACL TOP® Family, ACL™ ELITE/ELITE PRO® 8/9/10000 and ACL Futura/ACL Advance Systems). HemosIL UF Heparin Controls (Assayed): For the quality control of the HemosIL Liquid Heparin assay when testing for unfractionated heparin (UFH) on IL Coagulation Systems (ACL TOP® Family, ACL™ ELITE/ELITE PRO® 8/9/10000 and ACL Futura/ACL Advance Systems).
Test kit	Assayed quality control	Same
Matrix	Human plasma	Same
Number of levels	5 levels	Same

Differences		
Item	Device VALIDATE® Heparin Calibration Verification/Linearity Test Kit	Predicates HemosIL LMW Controls HemosIL UF Heparin Controls
Analyte	Heparin anti-Xa activity	LMW and UF heparin

K. Standard/Guidance Document Referenced:

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline–Third Edition

CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A statistical Approach; Approved Guideline

CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline

WHO International Standard 01/608, 2nd International Standard for Low Molecular Weight Heparin

WHO International Standard 97/578, 5th International Standard for Unfractionated Heparin

L. Test Principle:

The VALIDATE® Heparin Calibration Verification/Linearity Test Kit consists of assayed quality control materials used to establish the relationship between theoretical and actual performance of heparin anti-Xa activity.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision performance was evaluated on the IL ACL TOP® 500 analyzer. To obtain estimates of repeatability and within-laboratory precision, three lots of the VALIDATE® Heparin Calibration Verification/Linearity Test Kit (levels 1–5) were tested with one lot of HemosIL® Liquid Heparin reagents and quality controls. Testing was performed on one IL ACL TOP® 500 analyzer over 20 days, two runs per day, and two replicates per run to obtain a total of 80 replicates per kit level and lot. Estimates were expressed as %CV and SD for the within-run, between-run, between-day, and within-laboratory (total) variance components, as illustrated in the table below. Results for each level met the pre-determined acceptance criteria.

Level 1		**Mean IU/mL**	**Within-run**		**Between-run**		**Between-day**		**Total**	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Heparin Anti-Xa	Lot 1	0.101	0.010	10.3	0.007	6.7	0.000	0.0	0.012	12.3
	Lot 2	0.100	0.013	12.6	0.005	5.1	0.004	3.8	0.014	14.1
	Lot 3	0.098	0.010	10.7	0.003	3.4	0.004	4.1	0.012	12.0

Level 2		**Mean IU/mL**	**Within-run**		**Between-run**		**Between-day**		**Total**	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Heparin Anti-Xa	Lot 1	0.485	0.009	1.8	0.000	0.0	0.005	1.0	0.010	2.1
	Lot 2	0.480	0.007	1.4	0.009	1.9	0.008	1.7	0.014	2.9
	Lot 3	0.482	0.009	1.9	0.001	0.2	0.006	1.2	0.011	2.2

Level 3		**Mean IU/mL**	**Within-run**		**Between-run**		**Between-day**		**Total**	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Heparin Anti-Xa	Lot 1	0.899	0.012	1.3	0.011	1.3	0.009	1.0	0.018	2.1
	Lot 2	0.891	0.014	1.5	0.006	0.7	0.009	1.0	0.017	1.9
	Lot 3	0.879	0.012	1.4	0.013	1.4	0.010	1.1	0.020	2.3

Level 4		**Mean IU/mL**	**Within-run**		**Between-run**		**Between-day**		**Total**	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Heparin Anti-Xa	Lot 1	1.318	0.021	1.6	0.012	0.9	0.011	0.8	0.026	2.0
	Lot 2	1.298	0.018	1.4	0.016	1.2	0.016	1.2	0.029	2.2
	Lot 3	1.296	0.016	1.2	0.019	1.5	0.020	1.6	0.032	2.5

Level 5		Mean IU/mL	Within-run		Between-run		Between-day		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Heparin Anti-Xa	Lot 1	1.767	0.024	1.3	0.024	1.4	0.021	1.2	0.040	2.3
	Lot 2	1.742	0.018	1.0	0.014	0.8	0.031	1.8	0.038	2.2
	Lot 3	1.761	0.025	1.4	0.013	0.7	0.006	0.4	0.029	1.6

A single lot of VALIDATE® Heparin Calibration Verification/Linearity Test Kit (levels 1–5) was analyzed over five operating days, one run per day, and five replicates per run across multiple sites. Testing was performed on the IL ACL TOP® 500 analyzer. Estimates were expressed as %CV and SD for the within-run, within-laboratory, and reproducibility (total) variance components, as illustrated in the table below. Results for each level met the defined acceptance criteria.

Level	Mean IU/mL	Within-run		Within-Laboratory		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV
Level 1	0.099	0.007	6.9	0.011	10.9	0.015	15.0
Level 2	0.478	0.011	2.4	0.037	7.7	0.040	8.3
Level 3	0.887	0.016	1.9	0.053	6.0	0.054	6.1
Level 4	1.354	0.022	1.7	0.056	4.1	0.057	4.2
Level 5	1.819	0.031	1.7	0.049	2.7	0.060	3.3

b. Linearity/assay reportable range:

Linearity was verified on the IL ACL TOP® 500 instrument for the VALIDATE® Heparin Calibration Verification/Linearity Test Kit using three different lots. Results met the defined acceptance criteria.

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

Traceability:

The traceability of the IL HemosIL® heparin calibrator is traceable to the 5th International WHO Standard 97/578 for UF heparin and the 2nd International WHO Standard 01/608 for LMW heparin.

Shelf life and Open Vial Stability Testing:

A real-time stability study was performed to support the shelf-life claim for the VALIDATE® Heparin Calibration Verification/Linearity Test Kit. The real-time stability study was performed on the IL ACL TOP® 500 analyzer with four individual VALIDATE® Heparin Calibration Verification/Linearity Test Kit lots. The shelf-life claim was established at 5 months from the date of manufacture (DOM) when stored at -25°C to -10°C. Results for each level met the defined acceptance criteria.

A freeze/thaw stress stability study was conducted to support a maximum of two freeze/thaw events. Results for each level met the defined acceptance criteria.

Value Assignment:

A linear relationship exists between levels 1 through 5 of each VALIDATE® Heparin Calibration Verification/Linearity Test Kit; level 1 being the lowest concentration and level 5 being the highest concentration. Levels 1 and 5 are prepared independently by the addition of heparin to a human plasma base matrix. The heparin is sourced from a commercial manufacturer. Intermediate levels 2, 3, and 4 are subsequently prepared from levels 1 and 5 by equal part dilutions. Testing was performed for each level on five separate days with six replicates per day for a total of 30 replicates per level. Total percent coefficient of variation (%CV) was calculated for levels 1 and 5, and found to be within predefined acceptance criteria. Typical mean recovery values for one representative lot tested using the VALIDATE® Heparin Calibration Verification/Linearity Test Kit in combination with the IL ACL TOP® 500 analyzer are presented in the table below.

VALIDATE Heparin	Level 1	Level 2	Level 3	Level 4	Level 5
Heparin anti-Xa (IU/mL)	0.11	0.52	0.94	1.36	1.77

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:

   Not applicable

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.