510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K170864

B. Purpose for Submission:

To expand the use of previously cleared VALIDATE® D-Dimer Calibration Verification/Linearity Test Kit to the Siemens Sysmex CS-2500® instrument system in combination with Siemens INNOVANCE® D-Dimer reagent.

C. Measurand:

D-Dimer

D. Type of Test:

Quantitative

E. Applicant:

Maine Standards Company LLC

F. Proprietary and Established Names:

VALIDATE® D-Dimer 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(s):

   VALIDATE® D-Dimer 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 the following analyte: D-Dimer in a clinical laboratory setting by laboratory personnel. The product is intended for use with quantitative assays on the indicated analyzers specified in the labeling.

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   Siemens Sysmex CS-2500® instrument system and Siemens INNOVANCE® D-Dimer reagent (K151259)

   Diagnostica Stago STA-R® Evolution (K093001) and STA® - Liatest® D-Di (K162227)

   Instrumentation Laboratory (IL) ACL TOP Family and HemosIL® D-Dimer HS assay (K160276)

I. Device Description:

The VALIDATE® D-Dimer Calibration Verification/Linearity Test Kit consists of assayed quality control materials used to establish the relationship between theoretical and actual performance of the D-Dimer analyte. The kit includes five levels of D-Dimer analyte in a human plasma base matrix. VALIDATE® D-Dimer Calibration Verification/Linearity Test kit solutions are not intended for use as calibration materials.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VALIDATE® D-Dimer Calibration Verification/Linearity Test Kit

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

   K152961

3. Comparison with predicate:

Similarities		
Item	Device	Predicate (K152961)
	VALIDATE® D-Dimer Calibration Verification/Linearity Test Kit	VALIDATE® D-Dimer Calibration Verification/Linearity Test Kit
Intended Use	For *in vitro* diagnostic use in the quantitative determination of linearity, calibration verification and verification of reportable range for the following analyte: D-Dimer in a clinical laboratory setting by laboratory personnel. The product is intended for use with quantitative assays on the indicated analyzers specified in the labeling.	Same
Analyte	D-Dimer	Same
Stability	Shelf -life: Until expiration date printed on labeling Open-vial: maximum of 4 freeze/thaw cycles when stored at -10 to -25°C between cycles	Same
Matrix	Human plasma	Same
Number of Levels	5 Levels	Same
Preparation	Liquid; Ready to Use	Same
Storage	-10 to -25°C	Same

There is no difference between the subject device and the predicate.

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

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

CLSI EP06-A; Evaluation of Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

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

L. Test Principle:

The VALIDATE® D-Dimer Calibration Verification/Linearity Test Kit is used for calibration verification and verification of the D-dimer measuring range of the INNOVANCE® D-Dimer reagent with the Siemens Sysmex CS-2500® instrument system. The kit includes five levels of D-dimer used to establish the relationship between theoretical and actual performance of the D-Dimer analyte quantitatively. The Level 1 D-Dimer is configured to contain the lowest level (lower limit) and Level 5 D-Dimer to contain the highest level (upper limit) of concentration of D-Dimer of the measuring range. The intermediate levels (Level 2, Level 3, and Level 4) are subsequently prepared from Level 1 and Level 5 by equal part dilutions following the CLSI EP06-A guideline to measure intermediate levels of the measuring range.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was evaluated on the Siemens Sysmex CS-2500® instrument system with the VALIDATE® D-Dimer Calibration Verification/Linearity Test kit. One lot of VALIDATE® D-Dimer (levels 1–5) was tested with one lot of Siemens INNOVANCE® D-Dimer reagent and quality controls on three instruments, across multiple sites, over five days, with one run per day of each level, five replicates per run, and a minimum of three operators. The study produced a total of 75 data points for each level. The reproducibility study met the pre-specified acceptance criteria. Results from the study are provided in the table below:

Sample	Mean (mg/L FEU)	Repeatability		Within-Laboratory		Reproducibility	
		SD	%CV	SD	%CV	SD	%CV
Level 1	0.30	0.013	4.2%	0.013	4.4%	0.016	5.4%
Level 2	1.17	0.033	2.8%	0.043	3.6%	0.045	3.8%
Level 3	2.10	0.060	2.9%	0.099	4.7%	0.160	7.6%
Level 4	3.08	0.099	3.2%	0.180	5.8%	0.292	9.5%
Level 5	3.97	0.13	3.3%	0.294	7.4%	0.384	9.7%

b. Precision/Repeatability:

To evaluate repeatability and within-laboratory precision, three lots of VALIDATE® D-Dimer Calibration Verification/Linearity Test kit (levels 1–5) were tested with one lot of Siemens INNOVANCE® D-Dimer reagent and quality controls at one site on one Siemens Sysmex CS-2500® instrument system.The study was performed over 20 operating days, two runs per day, and two replicates per run with a minimum of two operators to obtain a total of 240 replicates for each level. The repeatability study met the pre-determined acceptance criteria. Results from the study are summarized in the table below:

Sample	N	Mean (mg/L FEU)	Within-Run		Between-Run		Between-Day		Between-Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Level 1	240	0.29	0.012	4.1%	0.001	0.5%	0.005	1.6%	0.006	2.0%	0.014	4.9%
Level 2	240	1.19	0.042	3.6%	0.000	0.0%	0.053	4.5%	0.000	0.0%	0.068	5.7%
Level 3	240	2.07	0.068	3.3%	0.029	1.4%	0.049	2.4%	0.000	0.0%	0.089	4.3%
Level 4	240	3.02	0.139	4.6%	0.087	2.9%	0.119	4.0%	0.000	0.0%	0.203	6.7%
Level 5	240	4.01	0.183	4.6%	0.131	3.3%	0.156	3.9%	0.000	0.0%	0.274	6.8%

c. *Linearity/assay reportable range:*

Linearity was determined using three lots of the VALIDATE® D-Dimer Calibration Verification/Linearity Test kit on the Siemens Sysmex CS-2500® instrument. Linearity performance was confirmed for the D-Dimer analyte using statistical software. The D-dimer concentrations of each measured value of the five levels were plotted vs. five assigned levels of concentration. The results were determined to be linear.

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

Stability:

Open Vial (Freeze/Thaw) Stability

A freeze/thaw vial stability assessment was performed to support the open vial stability claim. Three lots of the VALIDATE® D-Dimer Calibration Verification/Linearity Test kit were tested on a Siemens Sysmex CS-2500® instrument. The study demonstrated that each level of VALIDATE® D-Dimer is stable after four freeze/thaw events when stored at -10 to -25°C. The study met the pre-determined acceptance criteria.

Closed Vial Stability Study

Real-time stability testing was performed using three lots of VALIDATE® D-Dimer Calibration Verification/Linearity Test kit on a Siemens Sysmex CS-2500® instrument. Results from the VALIDATE® D-Dimer meet acceptance criteria out to a 2 month time point from the date of manufacture (DOM) when stored at -10 to -25°C. A 2 month expiry date is supported by current stability data. Real-time stability testing is ongoing. Stability data is being maintained to extend the stability claim of the VALIDATE® D-Dimer Calibration Verification/Linearity Test kit.

Expected Values:

Value Assignment/Recovery Data

Value assignment for the VALIDATE® D-Dimer Calibration Verification/Linearity Test kit is established by testing Level 1 (lowest concentration) and Level 5 (highest concentration) of VALIDATE® D-Dimer to generate 30 replicates on one Siemens Sysmex CS-2500® instrument. The value assignments for the intermediate levels are calculated based on an equal distance (delta) between levels. Levels 1 and 5 are prepared independently by the addition of D-dimer to a human plasma base matrix. Intermediate Levels 2, 3, and 4 are subsequently prepared from Levels 1 and 5 by equal part dilutions following CLSI EP06-A. The value assignment study met the pre-determined acceptance criteria. Typical recovery target values for all five levels are presented in the table below:

Instrument	**Analyte**	**Levels (mg/L FEU)**				
		1	2	3	4	5
Sysmex CS-2500®	D-Dimer	0.30	1.19	2.08	2.97	3.86

e. Detection limit:

Not applicable

f. Analytical specificity:

Not applicable

g. 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:

The VALIDATE® D-Dimer Calibration Verification/Linearity Test kit is manufactured such that a linear relationship exists among Levels 1 through 5. Actual expected values will be included in the kit lot Certificate of Analysis sheet for each Level 1 and Level 5. The values for mid-levels are calculated based on an equal distance (delta) between levels.

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.