



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

I Background Information:

A 510(k) Number

K213917

B Applicant

HemoSonics, LLC

C Proprietary and Established Names

QStat Cartridge

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QFR	Class II	21 CFR 864.5430 - Coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

Clearance of a new device

B Measurand:

Clot Time (CT), Clot Stiffness (CS), Fibrinogen Contribution to Clot Stiffness (FCS), Platelet Contribution to Clot Stiffness (PCS), and Clot Stability to Lysis (CSL)

C Type of Test:

Semi-quantitative

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The QStat Cartridge is a multi-channel cartridge that provides semi-quantitative indications of the coagulation and clot lysis state of a 3.2% citrated venous whole blood sample using the Quantra Hemostasis Analyzer. The QStat Cartridge includes tests to assess coagulation via the intrinsic and extrinsic pathways and includes a test with tranexamic acid to evaluate clot lysis characteristics.

The QStat Cartridge is intended for in vitro diagnostic use by trained professionals at the point-of-care and in clinical laboratories to evaluate the viscoelastic properties of whole blood by means of the following functional parameters: Clot Time (CT), Clot Stiffness (CS), Fibrinogen Contribution to Clot Stiffness (FCS), Platelet Contribution to Clot Stiffness (PCS), and Clot Stability to Lysis (CSL).

The QStat Cartridge is indicated for the evaluation of blood coagulation and clot lysis in patients age 18 years and older to assess possible hypocoagulable and hypercoagulable conditions in trauma and liver transplantation procedures.

Results obtained with the QStat Cartridge should not be the sole basis for patient diagnosis.

For prescription use only.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For in vitro diagnostic use

D Special Instrument Requirements:

Quantra Hemostasis Analyzer

IV Device/System Characteristics:

A Device Description:

The QStat Cartridge is a single-use, multi-channel disposable plastic cartridge used with the Quantra Hemostasis Analyzer to assess a patient's coagulation and clot lysis in a hospital setting (point of care or laboratory) during trauma and liver transplantation procedures. The QStat Cartridge consists of four independent channels that can be tested simultaneously with Sonic Estimation of Elasticity via Resonance (SEER) Sonorheometry.

Each QStat Cartridge is pre-filled with reagents individually sealed in an airtight pouch. After a QStat Cartridge is removed from its primary packaging, it is inserted into the Quantra

Hemostasis Analyzer instrument dock. A venous whole blood sample, collected in a 3.2% sodium citrate anticoagulant blood collection tube (minimum volume 2.7 mL), is attached directly to the cartridge and the test is initiated using the touch screen interface on the Quantra Hemostasis Analyzer. The cartridge is the only component of the Quantra system that is in direct contact with blood. The fluidic system within the instrument draws the sample into the cartridge where it is warmed to 37°C, aliquoted, introduced and mixed with the lyophilized reagents, and analyzed. When the test is complete, the cartridge is released from the dock to be disposed of in an appropriate biosafety sharps container.

Each channel of the cartridge contains prefilled lyophilized reagents in the form of beads that enable differential testing without the need for any reagent preparation or pipetting before testing. The assay provides the following information for each patient sample: Clot Time (CT), Clot Stiffness (CS), Fibrinogen Contribution to Clot Stiffness (FCS), Platelet Contribution to Clot Stiffness (PCS) and Clot Stability to Lysis (CSL).

QStat Cartridge Reagents and Test function per Channel

Channel	Reagents	QStat Cartridge Output Parameter (units of measure)
Measured Parameters		
1	Kaolin, calcium, buffers and stabilizers	Clot Time (CT) (seconds)
2	Thromboplastin, tranexamic acid (TXA), polybrene, calcium, buffers, and stabilizers	No direct output (see calculated parameters)
3	Thromboplastin, polybrene, calcium, buffers, and stabilizers	Clot Stiffness (CS) (hectopascals)
4	Thromboplastin, polybrene, abciximab, calcium, buffers, and stabilizers	Fibrinogen Contribution to Clot Stiffness (FCS) (hectopascals)
Calculated Parameters		
2 & 3	See above	Clot Stability to Lysis (CSL) (percent)
3 & 4	See above	Platelet Contribution to Clot Stiffness (PCS) (hectopascals)

The analyzer displays the test results in three different views: dial display screen, stiffness curves data, and trend screen. The dial display screen is the primary viewing screen and has a dial for each of the five output parameters. Each dial shows the reference range, assay measurement range, parameter abbreviation, and the numerical result for the corresponding parameter. The stiffness curves are a graphical display of shear modulus measurements over time that enable the user to view the development of clot stiffness over time. The trends screen displays results from a patient for up to six time points.

There are two levels of external QStat Controls (QSL1 and QSL2). QC is manufactured by HemoSonics and will be commercially available separately from the Quantra Hemostasis Analyzer and QStat Cartridge. The QSL1 and QSL2 are recommended to be run monthly, changing cartridge lots, changing control lots, or after significant changes are made to the Quantra instrument (e.g., software update). QSL1 and QSL2 are reconstituted by the end user with the provided diluent and loaded onto the QStat by the same method as patient samples. The

plastic diluent vial is shipped with an extender that serves to guide the vial into the cartridge's evacuated sample tube attachment, after reconstitution. The QStat Controls contain materials to test the measured output parameters for the QStat Cartridge: CT, CS, and FCS, as well as the calculated parameters, CSL and PCS.

The Quantra Cleaning Cartridge is an accessory for the Quantra Hemostasis Analyzer and is intended to be used for simple, periodic cleaning.

B Principle of Operation:

The QStat Cartridge uses Sonic Estimation of Elasticity via Resonance (SEER) Sonorheometry, a ultrasound-based technology, which uses ultrasound pulses to quantify the shear modulus (i.e., stiffness) of a blood sample during the process of coagulation and clot lysis. A focused ultrasound pulse is transmitted into the blood sample to generate a shear wave, causing the sample to resonate once the clot begins to form. Multiple parameters measured from the four channels of the cartridge provide information about the functional role of the coagulation factors, fibrinogen, platelets, and clot lysis factors in the sample.

Clot Time (CT) Test

CT is directly measured in Channel #1 using kaolin to provide contact surface activation of coagulation via the intrinsic pathway. Kaolin is an aluminum silicate mineral with a negatively charged surface. Calcium acetate is included to re-calcify the blood sample used for testing. Prolongation of the intrinsic pathway clot time is likely due to deficiencies in intrinsic pathway coagulation factors, presence of anticoagulants, or inhibitors that affect the intrinsic pathway.

Clot Stiffness (CS) Test

CS is directly measured in Channel #3 and is determined by measuring the stiffness after the clot has formed, using thromboplastin (tissue factor) to activate the extrinsic pathway of coagulation. The test includes polybrene, a reagent that neutralizes heparin. Calcium acetate is included to re-calcify the blood sample used for testing. This test allows an evaluation of the total clot stiffness from the combined contributions from both platelets and fibrinogen.

Fibrinogen Contribution to Clot Stiffness (FCS) Test

FCS is directly measured in Channel #4 using thromboplastin (tissue factor) to activate the extrinsic pathway of coagulation, in combination with a reagent that inhibits platelet aggregation and contraction (Abciximab). Abciximab is the Fab fragment of a monoclonal antibody that binds on the platelet surface receptor GPIIb/IIIa. Polybrene is included to neutralize heparin in addition to calcium acetate to re-calcify the blood sample used for testing. This test allows an evaluation of the contribution of functional fibrinogen to clot stiffness without the effect of heparin anticoagulation. In addition, when used in combination with the Clot Stiffness (CS) Test, the contribution of platelets to the clot stiffness can be determined.

Two additional functional parameters are calculated:

Platelet Contribution to Clot Stiffness (PCS)

PCS is a functional parameter that is calculated as the difference between the overall CS measured in Channel #3 and the FCS measured in Channel #4, reported in hectoPascals (hPa).

Clot Stability to Lysis (CSL)

CSL is a functional parameter that is calculated from Channel #2 and # 3 and is reported as a percent after the maximum stiffness in Channel #3 is detected. The CSL reports the loss in clot stiffness that is likely due to the influence of fibrinolysis on a scale from 100% (no clot lysis) to 10% (significant clot degradation).

V Substantial Equivalence Information:

A Predicate Device Name(s):

ROTEM *delta* Thromboelastometry System, EXTEM Assay, FIBTEM Assay, APTTEM Assay for the ROTEM *delta* Thromboelastometry System

B Predicate 510(k) Number(s):

K083842, K101533

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K213917</u>	<u>K083842</u>	<u>K101533</u>
Device Trade Name	QStat Cartridge	ROTEM® <i>delta</i> Thromboelastometry System	EXTEM® Assay, FIBTEM® Assay, APTTEM® Assay for the ROTEM® <i>delta</i> Thromboelastometry System
General Device Characteristic Similarities			
Intended Use/Indications For Use	The QStat Cartridge is a multi-channel cartridge that provides semi-quantitative indications of the coagulation and clot lysis state of a 3.2% citrated venous whole blood sample using the Quantra Hemostasis Analyzer. The QStat Cartridge includes tests to assess coagulation via the intrinsic and extrinsic pathways and includes a test with tranexamic acid to evaluate clot lysis characteristics. The QStat Cartridge is intended for in vitro diagnostic use by trained professionals at	The ROTEM® <i>delta</i> Thromboelastometry System is designed for in vitro diagnostic use by professionals in a laboratory environment. The ROTEM® <i>delta</i> is intended to provide a qualitative and quantitative indication of the coagulation state of a blood sample. For this purpose the ROTEM® <i>delta</i> records the clot firmness changes in a sample of citrated whole blood as the sample clots, retracts and lyses in real time. The analyzer output consists of a qualitative graphical	The EXTEM® assay is a semi-quantitative in vitro diagnostic assay used to monitor the coagulation process via the extrinsic pathway in citrated whole blood specimens on the ROTEM® <i>delta</i> Thromboelastometry System. Clotting characteristics are described by the functional parameters Clotting Time (CT), Speed of Clot formation (CFT and alpha angle), Clot Firmness (A20/MCF) and Clot Lysis (LOT, ML, LI(x)), CFT and alpha (Speed of Clot

	the point-of-care and in clinical laboratories to evaluate the viscoelastic properties of whole blood by means of the following functional parameters: Clot Time (CT), Clot Stiffness (CS), Fibrinogen Contribution to Clot Stiffness (FCS), Platelet Contribution to Clot Stiffness (PCS), and Clot Stability to Lysis (CSL). The QStat Cartridge is indicated for the evaluation of blood coagulation and clot lysis in patients age 18 years and older to assess possible hypocoagulable and hypercoagulable conditions in trauma and liver transplantation procedures. Results obtained with the QStat Cartridge should not be the sole basis for patient diagnosis. For prescription use only.	representation (mirrored coagulation curve – clot firmness over time) and several defined numerical parameters describing the curve quantitatively. The in-TEM® assay is a semi-quantitative <i>in vitro</i> diagnostic assay used to monitor the coagulation process via the intrinsic pathway in citrated whole blood specimens. Clotting characteristics are described by the functional parameters Clotting Time (CT), Speed of Clot formation (CFT and alpha angle), Clot Firmness (A20/MCF) and Clot Lysis (LOT, ML, LI(x)). The assay is intended for professional use in the clinical laboratory on the ROTEM® <i>delta</i> Instrument. The hep-TEM® assay is a semi-quantitative <i>in vitro</i> diagnostic assay used to monitor the coagulation process via the intrinsic pathway in the presence of heparin, in citrated whole blood specimens. Clotting characteristics are described by the functional parameters Clotting Time (CT), Speed of Clot formation (CFT and alpha angle), Clot Firmness (A20/MCF) and Clot Lysis (LOT, ML, LI(x)). The	Formation) are complementary parameters and should be used in conjunction with the main parameters Clotting Time (CT) and Clot Firmness (A20/MCF). The FIBTEM® assay is a semi-quantitative <i>in vitro</i> diagnostic assay on the ROTEM® <i>delta</i> Thromboelastometry System to monitor the clot firmness of a citrated whole blood specimen after blocking platelet contribution to the clot firmness. The fibTEM® is always used in conjunction with exTEM® Clotting characteristics are described by the functional parameter Clot Firmness (A20/MCF). The APTEM® assay is a semi-quantitative <i>in vitro</i> diagnostic assay on the ROTEM® <i>delta</i> Thromboelastometry System to monitor the clot firmness of a citrated whole blood specimen after blocking hyperfibrinolysis by aprotinin. The ap-TEM® is always used in conjunction with ex-TEM®. Clotting characteristics are described by the functional parameters Clotting Time (CT), Speed of Clot formation (CFT and alpha angle), Clot Firmness
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		assay is intended for professional use in the clinical laboratory on the ROTEM® <i>delta</i> Instrument. The NATEM® assay is a semi-quantitative <i>in vitro</i> diagnostic assay used to monitor the coagulation process contact activated by the surface of the measurement cell, in citrated whole blood specimens. Clotting characteristics are described by the functional parameters Clotting Time (CT), Speed of Clot formation (CFT and alpha angle), Clot Firmness (A20/MCF) and Clot Lysis (LOT, ML, LI(x)). The assay is intended for professional use in the clinical laboratory on the ROTEM® <i>delta</i> Instrument. The star-TEM® reagent is intended for use as recalcification reagent in the NATEM and in-TEM on the ROTEM® <i>delta</i> Thromboelastometry System.	(A20/MCF) and Clot Lysis (LOT, ML, LI(x)). CFT and alpha (Speed of Clot Formation) are complementary parameters and should be used in conjunction with the main parameters Clotting Time (CT) and Clot Firmness (A20/MCF). Each assay, APTEM, EXTEM and FIBTEM is performed on the ROTEM delta analyzer which has the following indication for use: The indication for ROTEM® delta is in adult patients when an evaluation of their blood coagulation properties is desired. Coagulation evaluations with the ROTEM® delta system are commonly used to assess clinical conditions in organ transplantation, cardiovascular surgery, cardiology procedures and trauma to assess post-operative hemorrhage and/or thrombosis.
Sample Type	3.2% sodium citrated whole blood	Citrated whole blood	Citrated whole blood
Results Display	Graphical (curves) and numerical display of patient results	Same	Same
Measurands	Clot time (CT)	Same	Same
	Clot Stiffness (CS)	Same Reported as EXTEM	Same Reported as EXTEM

		A20 (Clot Firmness)	A20 (Clot Firmness)
	Fibrinogen Contribution to Clot Stiffness (FCS)	Same Reported as FIBTEM A20	Same Reported as FIBTEM A20
Reagents (extrinsic pathway)	Thromboplastin	Same	Same
General Device Characteristic Differences			
Instrument	Quantra Hemostasis Analyzer	ROTEM® <i>delta</i> instrument	ROTEM® <i>delta</i> instrument
Sample Volume	3.0 mL citrated whole blood sample (2.7 mL whole blood + citrate)	300 µL per assay (in-TEM, hep-TEM, NATEM, star-TEM)	300 µL per assay (EXTEM, FIBTEM, APTEM)
Sample Preparation	Automated	Manual	Manual
Signal Generation	Ultrasonic pulses directed into a stationary well	Oscillating pin in stationary cup	Oscillating pin in stationary cup
Assay Output	Platelet Contribution to Clot Stiffness (PCS)	Output not directly provided but can be calculated offline from comparison of EXTEM and FIBTEM	Output not directly provided but can be calculated offline from comparison of EXTEM and FIBTEM
	Clot Stability to Lysis (CSL)	EXTEM and APTEM ML/LI60 and difference calculated offline.	EXTEM and APTEM ML/LI60 and difference calculated offline.
Reagents	Kaolin (intrinsic pathway activator)	Ellagic acid (intrinsic pathway activator)	Ellagic acid (intrinsic pathway activator)
	Abciximan (platelet inhibitor)	Cytochalasin D (platelet inhibitor)	Cytochalasin D (platelet inhibitor)
	Tranexamic acid (fibrinolysis inhibitor)	Aprotinin (fibrinolysis inhibitor)	Aprotinin (fibrinolysis inhibitor)
Principle of Operation	SEER Sonorheometry uses ultrasound pulses to quantify the shear modulus (i.e., stiffness) of a blood sample during the process of coagulation and clot lysis. A focused ultrasound pulse is transmitted into the blood sample to generate a shear wave, causing the sample to resonate once the clot	Shear elasticity of a coagulating sample by motion of an oscillating pin in a stationary cup. The motion of the pin is detected by an optical detection system. Data are processed and analyzed by a computer with special software.	Shear elasticity of a coagulating sample by motion of an oscillating pin in a stationary cup. The motion of the pin is detected by an optical detection system. Data are processed and analyzed by a computer with special software.

	begins to form.		
QC Materials	The Quantra Analyzer performs internal quality control checks of all system components at regular intervals and during each phase of a test run on a cartridge to verify that the instrument hardware and all subsystems are functioning properly. Two levels of external QStat Controls (Level 1 and Level 2) are available and supplied separately.	ROTOL N (Level 1) and ROTOL P (Level 2)	ROTOL N (Level 1) and ROTOL P (Level 2)

VI Standards/Guidance Documents Referenced:

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

CLSI EP07: *Interference Testing in Clinical Chemistry; Third Edition*

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

CLSI EP28-A3c: *Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition*

CLSI EP37: *Supplemental Tables for Interference Testing in Clinical Chemistry. First Edition*

VII Performance Characteristics (if/when applicable):

A. Analytical Performance:

1. Precision/Reproducibility:

a. *Single-site precision with Quantra QStat Controls*

A single-site precision study was performed over the course of 20 days, with two runs per day, and two replicates per run using QStat Control Level 1 (QSL1) and Level 2 (QSL2). A single Quantra Hemostasis Analyzer and a single lot of QStat Cartridges were utilized in the study, which was performed by a single operator. The results of this study demonstrated within-laboratory precision (total) of 0.0% – 9.5% CV for QSL1 and 0.6% – 9.3% CV for QSL2 parameters.

Single-site precision study with Quantra QStat Controls result summary:

QSL1										
Parameter	N	Mean	Repeatability		Between-Day		Between-Run		Total (Within-laboratory)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
CT (sec)	80	158.6	4.3	2.7	1.5	1.1	3.2	2.0	5.6	3.5
CSL(%)	80	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CS (hPa)	80	14.1	0.7	5.3	0.2	1.7	0.1	1.0	0.8	5.6
FCS (hPa)	80	14.7	1.3	8.6	0.4	2.6	0.5	3.2	1.4	9.5
PCS (hPa)*	80	< 0.2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
QSL2										
Parameter	N	Mean	Repeatability		Between-Day		Between-Run		Total (Within-laboratory)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
CT (sec)	80	269.9	16.0	5.9	4.2	1.6	0.0	0.0	16.6	6.1
CSL(%)	80	99.9	0.6	0.6	0.0	0.0	0.0	0.0	0.6	0.6
CS (hPa)	80	4.6	0.4	8.5	0.2	3.8	0.0	0.0	0.4	9.3
FCS (hPa)	80	4.7	0.4	7.9	0.2	3.3	0.1	2.7	0.4	9.0
PCS (hPa)*	80	< 0.2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

*QStat control materials do not contain platelets.

b. *Single-site precision with fibrinolysis positive controls*

A second single-site precision study was performed over the course of 20 days, with two runs per day, and two replicates per run using two levels of fibrinolysis positive samples, In-House Fibrinolytic Control (IHFC) Level 1 and Level 2. A single Quantra Hemostasis Analyzer and a single lot of QStat Cartridges were utilized in the study, which was performed by a single operator. The IHFC Level 1 includes 85 U/mL tissue plasminogen activator (tPA; targeting a borderline CSL (80-90%) at or near the threshold), whereas the IHFC Level 2 includes 140 U/mL tPA (targeting a lysis positive CSL value <60% and within the reportable range).

The results of this study demonstrated total %CV for CT, CS, and FCS below 5.8% across the two controls. For the CSL parameter, both the total %CV and total standard deviation (SD) were evaluated, with results demonstrating %CV of 7.1% and SD of 10.2% for the controls.

Single-site precision with fibrinolysis-positive controls results summary:

IHFC Level 1										
Parameter	N	Mean	Repeatability		Between-Day		Between-Run		Total (Within-laboratory)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
CT (sec)	80	224.8	8.4	3.7	2.4	1.1	0.0	0.0	8.7	3.9
CSL(%)	80	82.2	5.6	6.8	1.5	1.9	0.0	0.0	5.8	7.1
CS (hPa)	80	20.2	0.8	3.9	0.0	0.0	0.0	0.0	0.8	3.9
FCS (hPa)	80	20.9	0.6	2.9	0.2	1.0	0.2	0.7	0.7	3.2
PCS (hPa)*	80	< 0.2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

IHFC Level 2										
Parameter	N	Mean	Repeatability		Between-Day		Between-Run		Total (Within-laboratory)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
CT (sec)	80	219.8	11.6	5.3	12.7	5.8	5.3	2.4	12.7	5.8
CSL(%)	80	29.6	10.0	33.6	0.0	0.0	2.1	7.0	10.2	34.4
CS (hPa)	80	18.3	0.8	4.4	0.0	0.0	0.0	0.0	0.8	4.4
FCS (hPa)	80	19.5	0.9	4.5	0.2	0.9	0.0	0.0	0.9	4.6
PCS (hPa)*	80	< 0.2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

*IHFC materials do not contain platelets.

c. Multi-site precision study:

The multi-site precision study was performed over the course of five days at three external locations representative of intended user locations; POC laboratory, clinical research laboratory, and blood gas laboratory servicing operating rooms. During each day of testing, each sample was tested in duplicate by one operator per site on two Quantra instruments in parallel (n=4 total replicates per sample panel per day).

Testing was conducted with a panel of three whole blood samples on a single cartridge lot. Samples were created daily including one native normal sample and two contrived samples to evaluate different levels of fibrinolysis at and below the CSL threshold. The multi-site precision study demonstrated total imprecision of CSL parameter < 7% CV and <10 % CV for CT, CS, PCS, and FCS for normal and low tPA concentration (at CSL threshold).

All Sites – Sample 1 (unspiked)														
Parameter	N	Mean	Repeatability		Between-Day		Between-Analyzer		Within-Site		Between-Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CT	60	148.7	5.5	3.7	3.4	2.3	0.0	0.0	1.5	1.0	2.4	1.6	7.1	4.8
CSL	60	98.4	1.3	1.4	0.2	0.2	0.0	0.0	0.0	0.0	0.2	0.2	1.4	1.4
CS	60	21.3	1.0	4.5	0.5	2.3	0.6	3.0	0.0	0.0	0.7	3.2	1.4	6.7
PCS	60	19.5	1.0	4.8	0.4	2.0	0.6	3.3	0.0	0.0	0.8	3.9	1.4	7.3
FCS	60	1.9	0.1	5.5	0.1	5.9	0.0	0.0	0.0	0.0	0.1	4.9	0.2	9.1

All Sites – Sample 2 (tPA spiked to CSL threshold)														
Parameter	N	Mean	Repeatability (Replicate)		Between-Day		Between-Analyzer		Within-Site		Between-Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CT	60	129.6	8.4	6.5	3.7	2.9	0.0	0.0	0.0	0.0	0.0	0.0	9.2	2.9
CSL	60	85.1	3.6	4.2	2.8	3.3	0.0	0.0	1.1	1.3	2.8	3.3	5.5	6.4
CS	60	14.0	0.7	4.9	0.2	1.7	0.4	2.4	0.3	2.3	0.3	2.1	0.9	6.6
PCS	60	12.8	0.7	5.4	0.2	1.8	0.4	2.8	0.3	2.5	0.4	2.8	0.9	7.4
FCS	60	1.2	0.1	6.1	0.0	0.0	0.0	0.0	0.0	0.0	0.1	6.8	0.1	9.2

All Sites – Sample 3 (tPA spiked to below CSL threshold)														
Parameter	N	Mean	Repeatability (Replicate)		Between-Day		Between-Analyzer		Within-Site		Between-Site		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CT	60	132.8	6.9	5.2	1.3	0.9	0.0	0.0	3.5	2.6	0.0	0.0	7.9	5.9
CSL	60	22.0	8.8	40.1	2.6	12.0	0.0	0.0	1.7	7.9	0.0	0.0	9.4	42.6
CS	60	24.4	1.4	5.6	0.2	0.7	0.7	2.9	0.0	0.0	0.7	2.9	1.7	6.9
PCS	60	22.3	1.3	6.0	0.2	1.0	0.7	3.3	0.7	3.4	0.0	0.0	1.7	7.7
FCS	60	2.1	0.2	9.9	0.0	0.0	0.0	0.9	0.0	0.0	0.1	2.3	0.2	10.2

d. *Whole blood repeatability study:*

The whole blood repeatability study was evaluated using whole blood samples across multiple instruments, operators, and cartridge lots. Four separate studies were conducted that included testing a total of 16 samples, four native and 12 contrived samples, types including the following: normal (unspiked), fibrinolytic (CSL values between 18.7% and 99.3%), and hypocoagulable samples.

Study #1 evaluated the single source of variance between paired cartridges and instruments. Testing included a panel of seven samples including two non-contrived apparently healthy donors, three contrived fibrinolytic, one native hypocoagulable, and one contrived direct oral anticoagulant (DOAC) hypocoagulable samples. All samples were tested in duplicate on three cartridge lots with three matched instruments by two operators within a single day.

Study #2 evaluated the single source of variance between paired operators and instruments. Testing included a panel of four contrived fibrinolytic samples across the CSL reportable range. All samples were tested in duplicate on two cartridge lots per instrument across three instruments matched with three operators within a single day.

Study #3 included testing with 12 instruments run in parallel to eliminate variability introduced by using multiple aliquots of tPA. The study included a panel of three contrived fibrinolytic samples across the CSL reportable range. All samples were tested without instrument replicates on six different instruments per operator with three cartridge lots. Testing was conducted by two operators with 12 different instruments in total within a single day and therefore, two replicates per lot per operator.

Study #4 included testing with 12 instruments run in parallel to eliminate variability introduced by sample stability limitations of DOAC-based hypocoagulable samples. The study included a panel of two samples: one native hypocoagulable sample and one contrived DOAC hypocoagulable sample. Both samples were tested in duplicate per lot per operator with two cartridge lots. Testing was conducted by three operators with four different instruments per operator for a total of 12 instruments within a single day.

Variance analysis was performed using 12 results obtained from each sample type across the four studies. The results demonstrated total %CV below 15% for CT, CS, FCS, and

PCS across all sample types. For the CSL parameter, both the total %CV and total standard deviation (SD) were evaluated. The CSL %CV results were below 15% or SD below 12% across the various sample types and are summarized in the table below.

Whole Blood Repeatability Testing Summary: CSL												
Study 1												
Sample ID	N	Mean	Between - Replicate		Between-Operator		Between - Instrument/Cartridge Lot		Interaction Operator (Instrument/Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal WB	12	99.3	1.0	1.0	0.5	0.5	0.0	0.0	0.0	0.0	1.2	1.2
Normal WB	12	98.8	1.4	1.4	0.0	0.0	0.0	0.0	0.8	0.8	1.6	1.6
42 U/mL tPA	12	73.8	7.9	10.7	0.0	0.0	3.3	4.5	0.0	0.0	8.6	11.6
42.5 U/mL tPA	12	92.2	2.3	2.5	2.7	2.9	1.3	1.4	0.0	0.0	3.8	4.1
60 U/mL tPA	12	45.4	10.5	23.1	0.0	0.0	0.0	0.0	5.5	12.0	11.8	26.1
Apixaban 5 mg bidaily	12	97.8	2.5	2.5	0.0	0.0	0.0	0.0	4.4	4.5	5.1	5.2
Rivaroxaban 80 ng/mL	12	98.8	2.2	2.2	0.0	0.0	0.0	0.0	0.0	0.0	2.2	2.2

Whole Blood Repeatability Testing Summary: CSL												
Study 2												
Parameter	N	Mean	Between - Replicate		Between-(Operator/Instrument)		Between-Cartridge Lot		Interaction (Operator/Instrument) Cartridge Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
22.5 U/mL tPA	12	75.6	7.5	10.0	3.2	4.2	2.4	3.2	0.0	0.0	8.5	11.3
35 U/mL tPA	12	95.8	2.2	2.3	1.5	1.6	0.0	0.0	1.2	1.2	2.9	3.1
40 U/mL tPA	12	75.8	5.7	7.5	0.0	0.0	0.0	0.0	8.9	11.7	10.5	13.9
50 U/mL tPA	12	51.1	8.0	15.6	0.0	0.0	0.0	0.0	4.2	8.3	9.0	17.7

Whole Blood Repeatability Testing Summary: CSL												
Study 3												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
30 U/mL tPA	12	80.3	5.4	6.8	0.0	0.0	0.0	0.0	4.3	5.3	6.9	8.6
60 U/mL tPA	12	65.3	8.7	13.3	0.0	0.0	0.0	0.0	0.0	0.0	8.7	13.3
80 U/mL tPA	12	18.7	5.5	29.7	3.6	19.4	6.5	34.9	0.0	0.0	9.3	49.7

Whole Blood Repeatability Testing Summary: CSL												
Study 4												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Rivaroxaban 20 ng/mL	12	99.3	1.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	1.0
Dabigatran 300 ng/mL	12	98.3	1.7	1.8	0.0	0.0	0.0	0.0	1.5	1.5	2.3	2.3

Whole Blood Repeatability Testing Summary: CT												
Study 1												
Sample ID	N	Mean	Between - Replicate		Between-Operator		Between - Instrument/ Cartridge Lot		Interaction Operator (Instrument /Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal WB	12	154.2	4.3	2.8	1.1	0.7	5.4	3.5	0.0	0.0	7.0	4.5
Normal WB	12	123.8	6.8	5.5	0.0	0.0	2.0	1.6	0.0	0.0	7.1	5.8
42 U/mL tPA	12	148.6	8.1	5.5	0.0	0.0	4.0	2.7	0.0	0.0	9.1	6.1
42.5 U/mL tPA	12	137.6	5.5	4.0	6.8	5.0	5.5	4.0	0.0	0.0	10.3	7.5
60 U/mL tPA	12	155.2	11.6	7.5	3.1	2.0	2.9	1.8	0.0	0.0	12.3	8.0
Apixaban 5 mg bidaily	12	147.2	8.2	5.6	4.9	3.3	1.3	0.9	0.0	0.0	9.7	6.6
Rivaroxaban 80 ng/mL	12	191.5	9.7	5.1	2.2	1.1	0.0	0.0	1.8	0.9	10.1	5.3

Whole Blood Repeatability Testing Summary: CT												
Study 2												
Parameter	N	Mean	Between - Replicate		Between-Operator (Operator/ Instrument)		Between- Cartridge Lot		Interaction (Operator/ Instrument) Cartridge Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
22.5 U/mL tPA	12	142.7	8.5	6.0	0.9	0.7	2.3	1.6	0.0	0.0	8.9	6.2
35 U/mL tPA	12	140.7	9.9	7.1	4.9	3.5	0.0	0.0	0.0	0.0	11.1	7.9
40 U/mL tPA	12	128.8	4.7	3.6	2.4	1.9	0.0	0.0	4.0	3.1	6.6	5.1
50 U/mL tPA	12	157.2	8.1	5.1	0.0	0.0	0.0	0.0	5.3	3.4	9.7	6.1

Whole Blood Repeatability Testing Summary: CT												
Study 3												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between- Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
30 U/mL tPA	12	108.2	10.7	9.9	0.0	0.0	0.0	0.0	11.8	10.9	15.9	14.7
60 U/mL tPA	12	131.7	6.0	4.5	0.0	0.0	0.0	0.0	3.8	2.9	7.1	5.4
80 U/mL tPA	12	133.8	7.5	5.6	0.0	0.0	2.5	1.8	0.0	0.0	7.9	5.9

Whole Blood Repeatability Testing Summary: CT												
Study 4												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between- Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Rivaroxaban 20 ng/mL	12	224.1	7.6	3.4	15.8	7.0	5.8	2.6	0.0	0.0	18.5	8.2

Dabigatran 300 ng/mL	12	251.8	7.5	3.0	0.0	0.0	0.0	0.0	8.0	3.2	11.0	4.4
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Whole Blood Repeatability Testing Summary: CS												
Study 1												
Sample ID	N	Mean	Between - Replicate		Between-Operator		Between - Instrument/Cartridge Lot		Interaction Operator (Instrument /Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal WB	12	23.9	1.0	4.4	0.8	3.5	1.1	4.4	0.2	0.9	1.7	7.1
Normal WB	12	10.8	0.6	5.5	0.3	2.5	0.3	2.8	0.0	0.0	0.7	6.6
42 U/mL tPA	12	22.8	1.4	6.9	0.8	3.4	0.2	0.7	0.0	0.0	1.6	7.8
42.5 U/mL tPA	12	26.1	1.2	4.5	0.0	0.0	2.4	9.0	0.7	2.5	2.7	10.4
60 U/mL tPA	12	15.4	0.8	5.4	0.3	1.6	0.8	5.1	0.3	2.2	1.2	7.9
Apixaban 5 mg bidaily	12	14.2	1.0	6.9	0.0	0.0	0.0	0.0	1.7	11.7	1.9	13.6
Rivaroxaban 80 ng/mL	12	15.0	1.3	8.8	0.0	0.0	0.4	2.5	0.6	3.7	1.5	9.8

Whole Blood Repeatability Testing Summary: CS												
Study 2												
Parameter	N	Mean	Between - Replicate		Between-(Operator/Instrument)		Between-Cartridge Lot		Interaction (Operator/Instrument) Cartridge Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
22.5 U/mL tPA	12	19.9	0.8	4.1	0.0	0.0	0.0	0.0	0.8	4.2	1.2	5.8
35 U/mL tPA	12	21.3	1.0	4.6	0.4	1.6	1.0	4.9	0.3	1.2	1.5	7.0
40 U/mL tPA	12	14.4	0.5	3.3	0.7	4.5	0.6	3.9	0.6	3.9	1.1	7.8
50 U/mL tPA	12	25.8	1.0	3.7	0.5	1.8	0.1	0.2	0.0	0.0	1.1	4.2

Whole Blood Repeatability Testing Summary: CS												
Study 3												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
30 U/mL tPA	12	10.9	0.3	2.8	0.0	0.0	0.2	2.0	0.5	4.9	0.7	6.0
60 U/mL tPA	12	26.5	2.2	8.3	0.0	0.0	0.0	0.0	1.8	6.9	2.9	10.8
80 U/mL tPA	12	20.5	1.4	6.8	0.0	0.0	1.5	7.3	0.0	0.0	2.1	10.0

Whole Blood Repeatability Testing Summary: CS												
Study 4												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Rivaroxaban 20 ng/mL	12	19.2	6.0	31.1	0.0	0.0	2.1	11.1	1.9	10.0	6.6	34.5
Dabigatran 300 ng/mL	12	14.2	1.0	6.7	0.3	2.1	0.4	2.5	0.0	0.0	1.1	7.5

Whole Blood Repeatability Testing Summary: FCS												
Study 1												
Sample ID	N	Mean	Between - Replicate		Between-Operator		Between - Instrument/Cartridge Lot		Interaction Operator (Instrument /Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal WB	12	2.3	0.1	3.3	0.0	1.3	0.0	0.0	0.0	0.0	0.1	3.5
Normal WB	12	0.8	0.1	3.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	3.6
42 U/mL tPA	12	2.1	0.1	3.4	0.0	1.0	0.1	3.4	0.1	2.6	0.1	5.6
42.5 U/mL tPA	12	2.7	0.2	6.5	0.1	4.2	0.1	2.6	0.0	0.0	0.2	8.2
60 U/mL tPA	12	1.1	0.0	2.6	0.0	0.0	0.0	0.0	0.1	4.6	0.1	5.3
Apixaban 5mg bidaily	12	1.7	0.1	6.5	0.0	0.0	0.0	0.0	0.1	5.9	0.2	8.8
Rivaroxaban 80 ng/mL	12	1.3	0.1	3.8	0.0	3.1	0.1	6.0	0.0	1.5	0.1	7.9

Whole Blood Repeatability Testing Summary: FCS												
Study 2												
Parameter	N	Mean	Between - Replicate		Between-(Operator/Instrument)		Between-Cartridge Lot		Interaction (Operator/Instrument) Cartridge Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
22.5 U/mL tPA	12	2.4	0.2	7.6	0.0	0.0	0.0	0.0	0.1	3.3	0.2	8.3
35 U/mL tPA	12	2.3	0.1	2.8	0.1	3.1	0.0	0.0	0.0	1.3	0.1	4.4
40 U/mL tPA	12	1.4	0.1	4.9	0.0	2.0	0.0	0.0	0.0	0.0	0.1	5.3
50 U/mL tPA	12	2.5	0.1	5.4	0.0	0.0	0.0	0.0	0.0	0.0	0.1	5.4

Whole Blood Repeatability Testing Summary: FCS												
Study 3												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
30 U/mL tPA	12	0.6	0.0	4.5	0.0	0.0	0.1	7.8	0.0	0.0	0.1	9.0
60 U/mL tPA	12	2.9	0.3	11.8	0.1	4.3	0.1	3.7	0.0	0.0	0.4	13.1
80 U/mL tPA	12	1.9	0.2	7.9	0.0	0.0	0.1	2.6	0.0	0.0	0.2	8.4

Whole Blood Repeatability Testing Summary: FCS												
Study 4												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Rivaroxaban 20 ng/mL	12	2.3	0.4	16.1	0.3	12.7	0.0	0.0	0.1	4.2	0.5	20.9
Dabigatran 300 ng/mL	12	1.3	0.1	4.6	0.0	7.1	0.0	0.0	0.0	2.8	0.1	8.9

Whole Blood Repeatability Testing Summary: PCS												
Study 1												
Sample ID	N	Mean	Between - Replicate		Between-Operator		Between - Instrument/ Cartridge Lot		Interaction Operator (Instrument /Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Normal WB	12	21.5	0.9	4.4	0.8	3.8	1.1	5.0	0.3	1.2	1.7	7.7
Normal WB	12	10.0	0.6	5.9	0.3	2.6	0.3	3.1	0.0	0.0	0.7	7.1
42 U/mL tPA	12	20.7	1.4	6.9	0.7	3.4	0.3	1.3	0.0	0.0	1.6	7.8
42.5 U/mL tPA	12	23.3	1.3	5.4	0.0	0.0	2.4	10.4	0.5	2.3	2.8	11.9
60 U/mL tPA	12	14.3	0.8	5.8	0.3	1.9	0.8	5.7	0.3	2.3	1.2	8.6
Apixaban 5 mg bidaily	12	12.5	1.0	8.1	0.0	0.0	0.0	0.0	1.5	12.2	1.8	14.6
Rivaroxaban 80 ng/mL	12	13.7	1.3	9.7	0.0	0.0	0.5	4.0	0.5	3.3	1.5	11.0

Whole Blood Repeatability Testing Summary: PCS												
Study 2												
Parameter	N	Mean	Between - Replicate		Between-(Operator/ Instrument)		Between-Cartridge Lot		Interaction (Operator/ Instrument) Cartridge Lot		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
22.5 U/mL tPA	12	17.5	0.8	4.4	0.0	0.0	0.0	0.0	0.7	4.0	1.0	5.9
35 U/mL tPA	12	19.0	1.0	5.1	0.4	2.3	1.0	5.4	0.3	1.6	1.5	7.9
40 U/mL tPA	12	13.0	0.5	4.0	0.6	4.8	0.6	4.3	0.6	4.2	1.1	8.6
50 U/mL tPA	12	23.3	0.9	4.1	0.5	1.9	0.1	0.5	0.0	0.0	1.1	4.5

Whole Blood Repeatability Testing Summary: PCS												
Study 3												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
30 U/mL tPA	12	10.2	0.3	2.9	0.1	1.1	0.3	3.0	0.5	5.1	0.7	6.7
60 U/mL tPA	12	23.6	2.1	8.8	0.0	0.0	0.0	0.0	2.2	9.2	3.0	12.8
80 U/mL tPA	12	18.6	1.4	7.7	0.0	0.0	1.5	7.8	0.0	0.0	2.0	11.0

Whole Blood Repeatability Testing Summary: PCS												
Study 4												
Parameter	N	Mean	Between – Replicate		Between-Operator		Between-Cartridge Lot		Interaction Operator (Cartridge Lot)		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Rivaroxaban 20 ng/mL	12	16.9	5.7	34.0	0.0	0.0	2.1	12.6	2.3	13.5	6.5	38.7
Dabigatran 300 ng/mL	12	12.9	1.0	7.4	0.2	1.5	0.4	2.9	0.0	0.0	1.0	8.1

2. Linearity:

To assess the correlation between the QStat CSL parameter and tissue plasminogen activator (tPA) concentrations across the entire CSL reportable range, a dose-response study was performed. Five subjects were enrolled in the tPA dose-response study. For each enrolled subject, tPA was added to citrated whole blood samples to achieve final tPA concentrations of 0, 10, 30, 50, and 100 U/mL. Samples were tested in duplicate with the Quantra QStat Cartridge. A linear relationship was demonstrated between CSL and tPA concentrations.

3. Analytical Specificity/Interference:

The interference study evaluated the effect of potential interfering substances with normal whole blood and hypocoagulable tPA-treated whole blood. Each endogenous interferent was tested with normal whole blood and hypocoagulable tPA-treated whole blood.

Hypocoagulable specimens tested in the endogenous interference study consisted of:

- Fibrinolytic specimens (tPA-treated whole blood)
- Fibrinolytic specimens with additional hypocoagulable characteristics
 - o abciximab & tPA-treated whole blood
 - o tPA-treated low fibrinogen donor blood

If no interference was observed for normal whole blood and the three hypocoagulable specimen types an analyte was considered to not interfere up to the highest level tested, then no additional testing was performed.

The following table shows the highest concentration at which each substance showed no significant interference in whole blood samples collected in 3.2% sodium citrate anticoagulant collection tubes.

Potential Interferent	Concentration
Triglycerides / Lipid	1335 mg/dL
Hemoglobin	200 mg/dL
Hemolysis	Interfered at all levels tested (≥ 0.02 g/dL)
Lupus Anticoagulant	Interfered at all levels tested ($\geq 20\%$)
Clopidogrel	300 μ M
Salicylic Acid (Aspirin)	4.34 mM (69.4 mg/dL)
Protamine sulfate	20 μ g/mL
Tranexamic acid (TXA)	Normal blood: 60 μ g/mL Hypocoagulable tPA-treated blood: 1 μ g/mL
Clopidogrel (2-MeSAMP)	300 μ M
Protamine sulfate	Normal blood: 20 μ g/mL Hypocoagulable tPA-treated blood: 50 μ g/mL
EACA	600 μ g/mL Hypocoagulable tPA-treated blood: 10 μ g/mL
MPA	21 μ g/mL Hypocoagulable tPA-treated blood: 7 μ g/mL
Tacrolimus	144 ng/mL
Prednisone	99 ng/mL

Potential Interferent	Concentration
Rifaximin	40.5 ng/mL
Lactulose	12 µg/mL
Hemodilution (0–50% dilution with saline)	>10%
Dabigatran (Pradaxa)	25 ng/mL
Rivaroxaban (Xarelto)	25 ng/mL
Hematocrit	Normal whole blood (15.4–47.8% HCT): CT, CS, PCS, and FCS decreased with increasing hematocrit. No hematocrit interference occurred for CSL. Hypocoagulable whole blood (13. –55.3% HCT): CT, CS, PCS, and FCS decreased with increasing hematocrit. CSL increased with increasing hematocrit.

Sample Variable Interferences

Potential sources of interference due to sample collection variables were tested at one or more sample variable levels and compared to the control condition. The following potential sources of variability related to samples and sample preparation were evaluated: testing of first collected tube (discard tube) and under-filled tube (short draw).

Discard Tube:

The effect of omitting an initial discard tube (70–95 % normal volume) was evaluated by comparing results from an initial discard tube to results from a subsequent normal sample tube using Beckon Dickinson (BD) 2.7 mL tube. Discard tubes caused interference in CT, CS, PCS, and FCS relative to subsequent adequately filled sample tubes. Differences in results was noted between 0–18% in 9% of CS, PCS, and FCS results and 0–20% of 17% of CT results.

Short Draw/Under-filled Tube:

The effect of a short draw on the blood collection tube was evaluated by testing underfilled collection tubes at four levels ranging from 60%–90% of a typical tube fill. Collection of normal whole blood into the collection tubes was interrupted during the fill process to give tubes that were underfilled at 60%–90% of the specified normal fill and one tube filled to 100%. Testing was performed separately for 2.7 mL and 4.5 mL Becton Dickinson (BD) Vacutainer tubes (3.2% citrate). Short draw was found to interfere with QStat parameters at fill levels $\leq 80\%$ in BD 2.7 mL tubes and $\leq 70\%$ for the BD 4.5 mL tubes. Tests for which incomplete filling of the cartridge occurred due to insufficient sample volume ($\leq 70\%$ fill volume in 2.7 mL BD Vacutainer) triggered one or more internal quality control checks, resulting in no reported value.

4. Assay Reportable Range:

Validation that the QStat Cartridge parameters demonstrate functional performance across the claimed reportable ranges for each parameter was supported by data from the clinical validation study.

Output Parameter	Units	Reportable Ranges
Clot Time (CT)	Seconds	60 – 480

Output Parameter	Units	Reportable Ranges
Clot Stability to Lysis (CSL)	Percent	10 – 100
Clot Stiffness (CS)	hectoPascals	2 – 65
Platelet Contribution to Clot Stiffness (PCS)	hectoPascals	2 – 50
Fibrinogen Contribution to Clot Stiffness (FCS)	hectoPascals	0.2 -30

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Shelf-Life Cartridge Stability

The shelf-life reagent stability study includes three QStat Cartridge lots stored at 28°C (room temperature) and 2–8°C (refrigerated) with two levels of controls (QSL1 and QSL2), unspiked donor whole blood, and donor whole blood spiked with 100 IU/mL tPA. The cartridges were tested at time zero (T0) and every subsequent month up to 18 months. Shelf-life cartridge stability studies concluded unopened QStat Cartridge pouches can be stored up to 17 months after the date of manufacture at 2–28°C.

In-Use Reagent Stability

Cartridges are intended to be used shortly after opening (the foil pouch package), however a study was conducted to determine the stability of QStat Cartridge parameter measurements after the cartridge was opened compared to measurements from time 0, baseline measurement. Samples evaluated in this study were from the same whole blood donor tested in duplicate at 75% relative humidity and approximately 22°C. Results concluded QStat Cartridges are to be used within 15 minutes of opening.

Sample Stability

A sample stability study evaluated the stability of citrated whole blood for testing with the QStat Cartridge at ambient conditions (20–22°C) and in an incubator (28°C). A total of 17 native and contrived citrated whole blood specimens were evaluated for sample stability including normal whole blood as well as fibrinolytic and hypocoagulable whole blood samples. All sample types were tested at baseline (T0) and at intervals of 0.5, 1, 2, 4, and 5 hours after drawing. The study result supports the whole blood specimen stability is two hours after collection at 20–28°C.

Quality Control:

The Quantra Analyzer performs internal QC checks of all system components at regular intervals and during each phase of a test run on a cartridge to verify that the instrument hardware and all subsystems are functioning properly. There is no calibration material for the Quantra Hemostasis Analyzer, as user calibration is not required.

There are two levels of external QStat Controls – Level 1 (QSL1) and Level 2 (QSL2). The QStat Controls contain materials to test the measured output parameters for the QStat Cartridge: Clot Time (CT), Clot Stiffness (CS), and Fibrinogen Contribution to Clot Stiffness (FCS), as well as the calculated parameters, Clot Stability to Lysis (CSL), and Platelet Contribution to Clot Stiffness (PCS). The QSL1 and QSL2 do not include platelets; therefore, values for the CS parameter are expected to be at or below the reportable range (< 2 hPa). Value Assignment cards included in each control kit will provide the lot-specific

target ranges for the five Quantra output parameters. The Value Assignment is done by HemoSonics' procedure, as no standardized reference materials for the Quantra exist.

QSL1 and QSL2 vials are single-use only and should be stored refrigerated 2–8°C until use. When stored refrigerated, QSL1 and QSL2, should be allowed to warm to room temperature for at least 30 minutes before reconstituting.

QStat Quality Controls are recommended for use when changing QStat Cartridge lots, changing control lots, or after significant changes are made to the Quantra Hemostasis Analyzer.

Quality Control In-Use (Reconstituted) Stability Study

Reconstituted stability studies for QStat QC were evaluated using three lots of QSL1 and QSL2 and four lots of QStat Cartridges. Lyophilized QC lots were reconstituted following the instructions provided in the Instructions For Use for QStat controls. Controls were allowed to sit at room temperature during the 30-minute reconstitution time and during the study. Reconstituted controls were tested at baseline (30 minutes after reconstitution), and at time intervals for up to at least 2 hours after reconstitution. The in-use stability regression analysis supports the stability conclusions for QStat Level 1 and Level 2 Controls, for a minimum of 2 hours reconstituted stability at room temperature.

Quality Control Shelf-Life Stability Study

Three lots of QStat QC were evaluated to establish the shelf-life stability of the lyophilized QStat Quality Control materials when stored at 2–8°C. QC was tested at Time 0 and every subsequent month for a minimum of 13 months. When stored at 2–8°C, QStat Level 1 and 2 Controls are stable for 12 months.

6. Detection Limit:

Not applicable.

7. Assay Cut-Off:

Not applicable.

B. Comparison Studies:

1. Method Comparison with Predicate Device:

a. Comparison with ROTEM delta Thromboelastometry System:

The clinical performance of the QStat Cartridge and the predicate device, ROTEM delta Thromboelastometry System, was evaluated in a multi-center prospective observational study across 13 clinical sites in the US involving subjects 18 years of age or older. The study included 125 patients undergoing a liver transplant surgery, 159 trauma patients experiencing injuries requiring a full trauma response, and five normal subjects from which contrived samples were prepared.

From subjects undergoing liver transplant, a minimum of three blood samples were collected at the following times for analysis on the QStat Cartridge and the ROTEM®

delta Thromboelastometry System: before surgery, during the anhepatic phase, and post-reperfusion. For trauma subjects, at least one blood sample was collected in the emergency room, the operating room, or the intensive care unit at the time of admission, during acute hemorrhage and transfusion of blood products, or 24 to 48 hours after arrival at the trauma unit to assess potential hypercoagulability. Contrived samples (6.7%) were prepared by spiking blood samples from normal volunteers with fibrinogen and tPA to broaden the range of measurements for CS, FCS and CSL. All blood samples were run in parallel on the Quantra QStat Cartridge and the ROTEM delta.

Correlation and clinical agreement analyses were performed to compare measurements obtained with the QStat Cartridge to comparable measures obtained with the ROTEM delta Thromboelastometry System. A linear regression analysis was performed to evaluate the correlation between the QStat parameters and comparable ROTEM delta Thromboelastometry System parameters. For the primary analysis, samples from liver transplant and trauma subjects were combined with contrived samples. The results met the pre-defined acceptance criteria.

	N	Sample Range	Slope Estimate (95% CI)	Intercept Estimate (95% CI)	Correlation Coefficients	
					Pearson (95% CI)	Spearman (95% CI)
CT vs INTEM CT	448	66–479	0.37 (0.35, 0.39)	75.51 (69.90, 81.11)	0.89 (0.87, 0.91)	0.86 (0.83, 0.88)
CS vs EXTEM A20	540	2–52	2.84 (2.74, 2.94)	-1.46 (-2.14, -0.78)	0.92 (0.91, 0.93)	0.91 (0.90, 0.93)
FCS vs FIBTEM A20	539	0.2–12.9	3.08 (2.95, 3.21)	-0.30 (-0.45, -0.15)	0.89 (0.87, 0.91)	0.87 (0.85, 0.89)
PCS vs PLATEM	513	2.0–39.2	2.75 (2.43, 2.71)	0.33 (-0.45, 1.11)	0.93 (0.92, 0.94)	0.93 (0.92, 0.94)

A clinical agreement analysis was performed to evaluate the ability of the QStat CSL parameter to identify fibrinolytic samples relative to the comparable ROTEM® delta Thromboelastometry System lysis parameter EXTEM ML. The overall agreement of patient sample assignments into lysis-positive and lysis-negative based on data for QStat CSL and ROTEM delta EXTEM ML was 92.6%. Agreement within the lysis-positive and lysis-negative subcategories was 90.2% and 93.2%, respectively. These results met the acceptance criteria for overall and subcategory agreements.

Clinical Agreement Analysis for Comparison of QStat and ROTEM delta Lysis Parameters

ROTEM delta EXTEM ML				
QUANTRA QStat CSL		Lysis Positive*	Lysis Negative*	Total
	Lysis Positive**	83	28	111
	Lysis Negative**	9	381	390
	Total	92	409	501

**Classification based on Quantra definition of lysis

* Classification based on ROTEM definitions of lysis

Summary Metrics for Clinical Agreement Analysis for Comparison of QStat and ROTEM delta Lysis Parameters

Category	Agreement (95% CI)
Lysis Positive	0.90 (0.82, 0.95)
Lysis Negative	0.93 (0.93, 0.95)
Overall	0.93 (0.90, 0.95)

Linear Regression Summary: Liver Transplant Subjects

Eligible Liver Transplant Subject Set with 24 randomly selected Contrived Samples

	N	Sample Range	Slope Estimate (95% CI)	Intercept Estimate (95% CI)	Correlation Coefficients	
					Pearson (95% CI)	Spearman (95% CI)
CT vs INTEM CT	316	66–479	0.36 (0.37, 0.38)	85.52 (78.12, 92.92)	0.90 (0.86, 0.91)	0.85 (0.81, 0.88)
CS vs EXTEM A20	395	2–48.6	3.18 (3.08, 3.28)	-2.49 (-3.08, -1.91)	0.95 (0.94, 0.96)	0.91 (0.90, 0.93)
FCS vs FIBTEM A20	403	0.3–12.1	3.30 (3.16, 3.45)	-0.34 (-0.49, -0.19)	0.91 (0.89, 0.93)	0.88 (0.86, 0.90)
PCS vs PLATEM	374	2.1–36.5	2.97 (2.86, 3.08)	-1.30 (-1.83, -0.77)	0.94 (0.93, 0.95)	0.91 (0.89, 0.93)

Linear Regression Summary: Trauma Subjects

Eligible Trauma Subject Set with 12 randomly selected Contrived Samples

	N	Sample Range	Slope Estimate (95% CI)	Intercept Estimate (95% CI)	Correlation Coefficients	
					Pearson (95% CI)	Spearman (95% CI)
CT vs INTEM CT	163	68–273	0.58 (0.51, 0.65)	29.29 (17.69, 40.90)	0.80 (0.77, 0.83)	0.78 (0.76, 0.79)
CS vs EXTEM A20	144	2.4–52	2.82 (2.55, 3.08)	-2.85 (-5.02, -0.67)	0.87 (0.83, 0.91)	0.89 (0.85, 0.92)
FCS vs FIBTEM A20	142	0.2–9.7	3.18 (2.90, 3.46)	-0.72 (-1.07, -0.38)	0.88 (0.84, 0.91)	0.84 (0.79, 0.88)
PCS vs PLATEM	139	2.0–37.1	2.61 (2.36, 2.87)	-0.92 (-2.78, 0.95)	0.86 (0.81, 0.90)	0.89 (0.85, 0.92)

b. Comparison with the TEG 6S Hemostasis System (K183160)

At two clinical sites, 52 samples from trauma subjects were analyzed on the QStat Cartridge and the TEG 6S Hemostasis System. For the correlation analysis, TEG 6S clot stiffness amplitudes were first converted to units of clot elasticity (hPa). The limited data set was not supplemented with contrived samples.

	N	Sample Range	Slope Estimate (95% CI)	Intercept Estimate (95% CI)	Correlation Coefficients	
					Pearson (95% CI)	Spearman (95% CI)
CT vs CK-R	28	68–239	15.45 (12.15, 18.75)	46.49 (28.34, 64.64)	0.80 (0.67, 0.88)	0.81 (0.69, 0.88)
CS vs CK-MA	26	2.6–34.4	0.03 (0.03, 0.04)	-6.68 (-10.23, -3.78)	0.95 (0.88, 0.98)	0.93 (0.84, 0.97)
CS vs CRT-MA	26	2.0–30.4	0.03 (0.03, 0.04)	-7.01 (-9.74, -3.61)	0.95 (0.89, 0.98)	0.92 (0.83, 0.97)

FCS vs CFF-MA	26	0.2–4.0	0.13 (0.09, 0.17)	0.66 (-1.35 – 0.29)	0.82 (0.63, 0.92)	0.89 (0.78, 0.95)
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Clinical Agreement Analysis for Comparison of QStat Cartridge CSL and TEG 6S LY30

		TEG6S LY30		
QUANTRA QStat® CSL		Lysis Positive*	Lysis Negative*	Total
	Lysis Positive**	1	0	1
	Lysis Negative**	2	21	23
	Total	3	21	24

**Classification based on TEG6S definition of lysis (Lysis Positive if LY30 was > 2.6%)

* Classification based on ROTEM definitions of lysis

Overall, the agreement between QStat CSL and TEG 6S LY30 was 91.7% (with 95% CI of 0.73, 0.99).

2. Matrix Comparison:

Not applicable

C. **Clinical Studies:**

a. Clinical Sensitivity:

Not applicable

b. Clinical Specificity:

Not applicable

c. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Reader Study

A reader study was conducted to assess the ability of potential users of Quantra System with the QStat Cartridge to correctly interpret results displayed on the Quantra Dials Display and Curve screens. The QStat Reader Study was conducted with a total of 10 readers who regularly assess the blood coagulation status of patients in the critical care setting. Participants viewed 12 QStat results display screens, each containing results for five QStat Cartridge parameters, and answered a total of 131 multiple-choice questions. For all five QStat parameters, >95% of the questions pertaining to each of the displays were answered correctly.

D. **Clinical Cut-Off:**

Not applicable.

E. **Expected Values/Reference Range:**

The reference range study was a multi-center study aimed at establishing reference range intervals for a healthy population for the test parameters measured by the QStat Cartridge on the Quantra Hemostasis Analyzer. The study population consisted of 155 healthy men and women volunteers (≥18 years of age) enrolled across four external sites that are representative of the general population in the United States.

Output Parameter	Units	N	Reference Ranges
Clot Time (CT)	Seconds	150	121 – 175
Clot Stability to Lysis (CSL)	Percent	151	92 – 100*
Clot Stiffness (CS)	hectoPascals	151	14.0 – 35.4
Platelet Contribution to Clot Stiffness (PCS)	hectoPascals	153	12.8 – 32.3
Fibrinogen Contribution to Clot Stiffness (FCS)	hectoPascals	149	0.9 – 4.2

*The Clot Stability to Lysis (CSL) is a calculated parameter. CSL values of 92%–100% are demonstrated to be typical of “normal” patient samples. Samples with CSL values below 90% are indicative of reduction of clot stiffness that is likely due to the influence of fibrinolysis. The 90% threshold was calculated as the lower bound of the 95% confidence interval around the lower limit of the reference interval for CSL determined in healthy volunteers.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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