November 29, 2022

HemoSonics, LLC
Garrett Sparks
Regulatory Affairs
400 Preston Avenue, Suite 250
Charlottesville, Virginia 22903

Re: K213917
Trade/Device Name: QStat® Cartridge
Regulation Number: 21 CFR 864.5430
Regulation Name: Coagulation system for the measurement of whole blood viscoelastic properties in perioperative patients
Regulatory Class: Class II
Product Code: QFR
Dated: December 15, 2021
Received: December 15, 2021

Dear Garrett Sparks :

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the lectronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Min Wu -S

Min Wu
Branch Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

Device Name
QStat® Cartridge

Indications for Use *(Describe)*

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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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SECTION 5: 510(K) SUMMARY

510(k) SUMMARY

A. 510(k) NUMBER:

K213917

B. PURPOSE OF SUBMISSION

Clearance of a new assay

C. 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)

D. TYPE OF TEST

Sonic Estimation of Elasticity via Resonance (SEER) Sonorheometry to measure the shear modulus of whole blood during coagulation and clot lysis, semi-quantitative

E. APPLICANT

HemoSonics, LLC

F. PROPRIETARY AND ESTABLISHED NAMES

QStat® Cartridge

G. REGULATORY INFORMATION

1. Regulation Section:
   21 CFR 864.5430 - Coagulation System For The Measurement Of Whole Blood Viscoelastic Properties

2. Classification:
   Class II

3. Product Code:
   QFR – Coagulation System For The Measurement Of Whole Blood Viscoelastic Properties

4. Panel:
   Hematology (81)

H. INTENDED USE

1. Intended use(s):

   See Indications for use below

2. 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 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.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Quantra Hemostasis Analyzer

I. DEVICE DESCRIPTION

The QStat Cartridge is a single-use, multi-channel (n=4) disposable plastic cartridge used with the Quantra Hemostasis Analyzer to assess a patient's coagulation and clot lysis (possible hypocoagulable and hypercoagulable conditions) 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 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). The following table summarizes the lyophilized reagents contained in the QStat Cartridge and the test function for each cartridge channel and the output parameter.

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 (n=5) 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 six 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) that are supplied separately (required but not provided materials) for testing on the Quantra System when changing cartridge lots, changing control lots, or after significant changes are made to the Quantra instrument (e.g., software update).

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

J. SUBSTANTIAL EQUIVALENCE INFORMATION

1. Predicated Device Name:

   ROTEM Delta Thromboelastometry System

2. Predicate 510(k) Numbers:

   K083842 and K101533

3. Comparison with Predicate:

	QStat Cartridge (Proposed Device)	**ROTEM Delta Thromboelastometry System K083842 and K101533 (Predicates)**
Intended 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	***K083842*** The ROTEM® delta Thromboelastometry System is designed for in vitro diagnostic use by professionals in a laboratory environment. The ROTEM® delta is intended to provide a qualitative and quantitative indication of the coagulation state of a blood sample. For this purpose, the ROTEM® delta 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 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 in vitro diagnostic assay used to monitor the coagulation process via the intrinsic pathway in citrated whole

	QStat Cartridge (Proposed Device)	ROTEM Delta Thromboelastometry System K083842 and K101533 (Predicates)
	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.	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® delta Instrument. The hep-TEM® assay is a semi-quantitative in vitro 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 assay is intended for professional use in the clinical laboratory on the ROTEM® delta Instrument. The NATEM® assay is a semi-quantitative in vitro 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® delta Instrument. The star-TEM® reagent is intended for use as recalcification reagent in the NATEM and in-TEM on the ROTEM® delta Thromboelastometry System.
		K101533 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® delta 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 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 in vitro diagnostic assay on the ROTEM® delta

	QStat Cartridge (Proposed Device)	ROTEM Delta Thromboelastometry System K083842 and K101533 (Predicates)
		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 in vitro diagnostic assay on the ROTEM® delta 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 (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).
Similarities		
Classification	II	Same
Indications for Use	Trauma and liver transplantation	Trauma, organ transplantation, cardiovascular surgery, and cardiology procedures
Technological Purpose	Measuring “clot stiffness” during clot formation	Measuring “clot firmness” during clot formation
Measuring Channels	4	Same
Sample Type	3.2% sodium citrated whole blood	Same
Results Display	Graphical (curves) and numerical display of patient results	Same
Measurands	Clot time (CT)	Same
	Clot Stiffness (CS)	Same. Reported as EXTEM A20 (clot firmness)
	Fibrinogen Contribution to Clot Stiffness (FCS)	Same Reported as FIBTEM A20
Reagents	Thromboplastin (extrinsic pathway)	Same
Differences		
Instrument	Quantra Hemostasis Analyzer	ROTEM *delta* instrument
Sample Volume	3.0 mL citrated whole blood sample (2.7 mL whole blood + citrate)	300 µL citrated whole blood sample per assay (INTEM, EXTEM, FIBTEM, APTEM)
Sample Preparation	Automated	Manual

	QStat Cartridge (Proposed Device)	ROTEM Delta Thromboelastometry System K083842 and K101533 (Predicates)
Signal Generation	Ultrasonic pulses directed into a stationary well	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
	Clot Stability to Lysis (CSL)	EXTEM and APTEM ML/LI60 and difference calculated offline.
Reagents	Kaolin (intrinsic pathway activator)	Ellagic acid (intrinsic pathway activator)
	Abciximab (platelet inhibitor)	Cytochalasin D (platelet inhibitor)
	Tranexamic acid (fibrinolysis inhibitor)	Aprotinin (fibrinolysis inhibitor)

K. STANDARDS/GUIDANCE DOCUMENTS REFERENCED

- CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline Second 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

L. TEST PRINCIPLE

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 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

This test uses 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 recalcify 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

This test uses thromboplastin (tissue factor) to activate the extrinsic pathway of coagulation. The test includes polybrene, a reagent that neutralizes heparin. Calcium acetate is included to recalcify 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
This test uses 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 recalcify 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)
The Platelet Contribution to Clot Stiffness (PCS) is a functional parameter that is calculated as the difference between the overall Clot Stiffness (CS) and the Fibrinogen Contribution to Clot Stiffness (FCS), reported in hectoPascals (hPa).

Clot Stability to Lysis (CSL)
The Clot Stability to Lysis (CSL) is a functional parameter defined as the normalized difference of the clot stiffness change after maximum clot stiffness in the absence of tranexamic acid and the corresponding clot stiffness change in the presence of tranexamic acid. The CSL parameter may indicate the reduction of clot stiffness that is likely due to the influence of fibrinolysis. The CSL parameter is reported in %.

M. PERFORMANCE CHARACTERISTICS

1. Analytical Performance

a. Precision/Reproducibility

i. Single Site Precision

The single site precision study included testing of the QStat Control Level 1 (QSL1) and QStat Control Level 2 (QSL2) in duplicate with 2 runs per day over 20 testing days. All sample testing was conducted using one Quantra instrument and reagent lot for cartridge and controls. Analysis of the Single Site Precision Study data for the QStat cartridge demonstrated within-laboratory precision (total) of 0.0% – 9.5% CV for QSL1 and 0.6% – 9.3% CV for QSL2 parameters. The repeatability for the QStat cartridge on the Quantra showed a replicate precision of 0.0% – 8.6% CV for QSL1 and 0.6% – 8.5% CV for QSL2 parameters. The results are summarized below.

QSL1 (N=80)									
Parameter	**Mean**	**Repeatability (Replicate)**		**Between-Day**		**Between- Run**		**Total**	
		SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
CT (sec)	158.6	4.3	2.7	1.5	1.1	3.2	2.0	5.6	3.5
CSL (%)	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
CS (hPa)	14.09	0.74	5.3	0.24	1.7	0.14	1.0	0.79	5.6
FCS (hPa)	14.69	1.26	8.6	0.38	2.6	0.47	3.2	1.4	9.5
PCS (hPa)*	< 0.2	NA	NA	NA	NA	NA	NA	NA	NA
QSL2 (N=80)									
Parameter	**Mean**	**Repeatability (Replicate)**		**Between-Day**		**Between- Run**		**Total**	
		SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
CT (sec)	269.9	16.0	5.9	4.2	1.6	0.0	0.0	16.6	6.1
CSL (%)	99.9	0.6	0.6	0.0	0.0	0.0	0.0	0.6	0.6
CS (hPa)	4.62	0.39	8.5	0.17	3.8	0.0	0.0	0.43	9.3
FCS (hPa)	4.69	0.37	7.9	0.15	3.3	0.12	2.7	0.42	9.0
PCS (hPa)*	< 0.2	NA	NA	NA	NA	NA	NA	NA	NA

**QStat Control materials do not contain platelets*

A second single site precision study was also performed with two levels of fibrinolysis-positive control materials (developed only for internal use at HemoSonics) prepared to simulate two different levels of fibrinolysis over the reportable range of the CSL parameter. Results from 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.

ii. Multi-Site Reproducibility

A multi-site repeatability and reproducibility study performed at three external clinical sites that were selected to represent different intended user locations. Testing was conducted with a panel of three whole blood samples over five days with two Quantra Analyzers per site and a single reagent lot. Samples were created daily including one native sample and two contrived samples to evaluate different levels of fibrinolysis at and below the CSL threshold (spiked with tissue-type plasminogen activator (tPA)). The results across all sites per sample type are summarized in the table below. Total imprecision of CSL parameter was < 7% CV for normal and low tPA concentration (at CSL threshold).

All Sites - Sample 1 (unspiked)														
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	148.7	5.52	3.71	3.39	2.28	0	0	1.45	0.97	2.42	1.63	7.06	4.75
CSL	60	98.38	1.33	1.35	0.24	0.24	0	0	0	0	0.2	0.2	1.37	1.39
CS	60	21.33	0.96	4.49	0.49	2.3	0.63	2.95	0	0	0.68	3.2	1.42	6.66
PCS	60	19.48	0.94	4.8	0.39	1.99	0.64	3.3	0	0	0.76	3.92	1.42	7.3
FCS	60	1.85	0.1	5.47	0.11	5.94	0	0	0	0	0.08	4.29	0.17	9.14
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	129.62	8.43	6.5	3.74	2.89	0	0	0	0	0	0	9.22	2.89
CSL	60	85.07	3.58	4.21	2.84	3.34	0	0	1.06	1.25	2.82	3.31	5.47	6.44
CS	60	13.95	0.69	4.93	0.24	1.71	0.36	2.58	0.32	2.33	0.29	2.11	0.92	6.61
PCS	60	12.75	0.68	5.36	0.23	1.83	0.36	2.81	0.32	2.5	0.36	2.81	0.94	7.35
FCS	60	1.2	0.07	6.14	0	0	0	0	0	0	0.08	6.78	0.11	9.15
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	5.22	1.25	0.94	0	0	3.49	2.63	0	0	7.86	5.92
CSL	60	21.97	8.8	40.07	2.64	12.01	0	0	1.73	7.88	0	0	9.35	42.56
CS	60	24.38	1.36	5.56	0.17	0.7	0.7	2.87	0	0	0.7	2.86	1.69	6.92
PCS	60	22.25	1.34	6.03	0.22	0.97	0.73	3.27	0.74	3.35	0	0	1.71	7.69
FCS	60	2.13	0.21	9.91	0	0	0.02	0.88	0	0	0.05	2.29	0.22	10.21

iii. Whole blood repeatability

The precision of the QStat Cartridge on the Quantra was evaluated using whole blood samples across multiple instruments, operators, and cartridge lots. Four separate studies were conducted that included testing a total 16 native and contrived sample 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 (normal, fibrinolytic and hypocoagulable) tested in duplicate on three reagent lots with three instruments and multiple 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 ranging from hyperfibrinolysis to normal fibrinolysis. Samples were tested in duplicate with two lots per instrument (n=3) and 3 operators within a single day.

Study #3 included testing with 12 instruments in parallel to eliminate variability introduced by contriving samples using multiple aliquots of tPA. Testing included a panel of three contrived fibrinolytic samples across the

CSL reportable range. All samples were tested in duplicate using three lots across six different instruments per operator (n=2).

Study #4 included testing with 12 instruments run in parallel to eliminate variability introduced by sample stability limitations of DOAC-based hypocoagulable samples. Testing included a panel of two hypocoagulable samples in duplicate per lot per operator with two cartridge lots by three operators with four different instruments per operator within a single day.

Variance analysis was performed using 12 results obtained from each sample type across the three 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.

CSL Variance Analysis for Whole Blood Repeatability Testing

Sample ID	Study	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	1	12	99.3	1.0	1.0	0.5	0.5	0.0	0.0	0.0	0.0	1.2	1.2
Normal	1	12	98.8	1.4	1.4	0.0	0.0	0.0	0.0	0.8	0.8	1.6	1.6
42.5 U/mL tPA	1	12	92.2	2.3	2.5	2.7	2.9	1.3	1.4	0.0	0.0	3.7	4.1
42 U/mL tPA	1	12	73.8	7.9	10.7	0.0	0.0	3.3	4.5	0.0	0.0	8.6	11.6
60 U/mL tPA	1	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	1	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	1	12	98.8	2.2	2.2	0.0	0.0	0.0	0.0	0.0	0.0	2.2	2.2
Sample ID	**Study**	**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%**
35 U/mL tPA	2	12	95.8	2.2	2.3	1.5	1.6	0.0	0.0	1.2	1.2	2.9	3.1
22.5 U/mL tPA	2	12	75.6	7.5	10.0	3.2	4.2	2.4	3.2	0.0	0.0	8.5	11.3
40 U/mL tPA	2	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	2	12	51.1	8.0	15.6	0.0	0.0	0.0	0.0	4.2	8.3	9.0	17.7
Sample ID	**Study**	**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	3	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	3	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	3	12	18.7	5.5	29.7	3.6	19.4	6.5	34.9	0.0	0.0	9.3	49.7
Rivaroxaban 20 mg daily	4	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	4	12	98.3	1.7	1.8	0.0	0.0	0.0	0.0	1.5	1.5	2.3	2.3

b. Linearity

Not Applicable.

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

Shelf-Life Reagent Stability
Unopened QStat Cartridge pouches may be stored up to 17 months after the date of manufacture at 2-28°C.

In-Use Reagent Stability
Recommend testing within 15 minutes after removing QStat Cartridge from its primary package pouch.

Specimen Stability
A total of n=13 native and contrived whole blood samples were evaluated for sample stability including normal whole blood as well as fibrinolytic and hypocoagulable whole blood samples. Fresh blood kept at room temperature should be analyzed within 2 hours after collection.

Controls
The QSL1 and QSL2 are single use vials containing a lyophilized mixture of porcine and caprine pooled animal plasma (3.2% sodium citrate), fixed red blood cells of human origin, buffers, additives, and preservatives (no platelets). 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.

d. Detection limit:

Not Applicable.

e. Analytical specificity:

The Interference Study evaluated the effect of potential interfering substances with normal whole blood and hypocoagulable whole blood. Interference was evaluated with unspiked ("Control") and at one or more spiked levels ("Test"). Screening studies were performed at one or two levels with the number of replicates at each level generally selected to provide a 95% confidence interval (2-sided), per CLSI EP07-A2 guidelines. Dose-response studies were also performed.

The following endogenous interferences were evaluated with a screening study: lipid, hemolysis, and hemoglobin. In addition, lupus anticoagulant, hemodilution, and hematocrit were evaluated as potential endogenous interferents with a dose-response study to determine the relationship between the test levels and their effects on the QStat Cartridge results.

The study also evaluated the potential effects of the following exogenous interferences: tranexamic acid (TXA), epsilon-aminocaproic acid (EACA), clopidogrel (2-MeSAMP), and aspirin (salicylic acid, sodium salt) in screening studies. In addition, dabigatran (Pradaxa), rivaroxaban (Xarelto), protamine sulfate, mycophenolic acid (MPA), tacrolimus, prednisone, rifaximin, and lactulose were evaluated as potential exogenous interferents in dose-response studies performed at multiple levels. The effects of potential sample variable interferences such as the use of discard tube and short draw were also evaluated. 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.

Interferent	Concentration
Lipid	1335 mg/dL
Hemolysis	Interfered at all levels tested (≥0.02 g/dL)
Hemoglobin	0.2 g/dL
Lupus Anticoagulant	Interfered at all levels tested (≥20%)
Clopidogrel	300 µM (highest level tested)
Aspirin	4.34 mM (0.694 mg/mL) (highest level tested)
Protamine sulfate	20 µg/mL
Mycophenolic Acid	7 µg/mL
Tacrolimus	144 ng/mL (highest level tested)
Prednisone	99 ng/mL (highest level tested)
Rifaximin	40.5 ng/mL (highest level tested)
Lactulose	12 µg/mL (highest level tested)

As expected and designed for, the following substances showed significant effects on QStat parameters. The anti-fibrinolytic agents TXA and EACA demonstrated an effect at concentrations greater than 1 µg/mL and 10 µg/mL respectively in fibrinolytic samples. The direct oral anticoagulants rivaroxaban and dabigatran demonstrated a dose response effect at concentrations greater than 25 ng/mL. Hemodilution demonstrated a dose response effect at dilutions greater than 10%. Increasing hematocrit levels in the range of 13 to 55% generated a decrease in most QStat results with effects starting at hematocrit changes of >2%.

Specimen collection tubes filled at less than 80% of the required/specified volume may affect results or cause incomplete filling of the QStat Cartridge. Use of a discard tube may affect QStat results.

2. Comparison Studies:

a. Method Comparison with predicate device:

The clinical performance of the Quantra Hemostasis Analyzer with the QStat Cartridge with the predicate device, ROTEM delta, was evaluated in a multi-center prospective observational study involving subjects 18 years of age or older undergoing liver transplant surgery or experiencing major trauma requiring a full trauma team response. Two hundred eighty-nine adult subjects were eligible for this study across thirteen clinical sites in the US including 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: 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. Trauma severity was assessed by injury scores in 71% of trauma subjects. For the majority of subjects (68%), the injury score was reflective of severe trauma. 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. A linear regression analysis was performed to evaluate the correlation between the QStat parameters and comparable ROTEM delta parameters. For the primary analysis, samples from liver transplant and trauma subjects were combined with contrived samples.

	Slope Estimate (95% CI)	**Intercept Estimate (95% CI)**	**Correlation Coefficients**	
			Pearson (95% CI)	**Spearman (95% CI)**
CT vs INTEM CT	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	2.84 (2.74, 2.94)	-1.46 (-2.16, -0.78)	0.92 (0.91, 0.93)	0.91 (0.90, 0.93)
FCS vs FIBTEM A20	3.08 (2.95, 3.21)	-0.30 (-0.45, -0.15)	0.89 (0.87, 0.91)	0.87 (0.85, 0.89)

A clinical agreement analysis was performed to evaluate the ability of the QStat CSL parameter to identify fibrinolytic samples relative to the ROTEM delta 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. The QStat CSL parameter appeared

to be more sensitive at identifying moderate fibrinolytic samples than the ROTEM delta lysis parameter.

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

		ROTEM delta		
		Yes*	**No***	**Total**
QUANTRA QStat	**Yes****	83	28	111
	No**	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	N in Category Quantra/ROTEM	Agreement (95% CI)
Yes	83/92	0.90 (0.82, 0.95)
No	381/409	0.93 (0.90, 0.95)
Overall	464/501	0.93 (0.90, 0.95)

b. Matrix Comparison

Not Applicable.

3. Clinical Studies:

Not applicable.

4. Clinical Cut-Off:

See reference range study below for CSL cutoff description.

5. Expected Values/Reference Range:

The reference range study was a multi-center, prospective, observational study aimed at establishing reference range intervals for a healthy population for the test parameters measured by the QStat Cartridge. The study population consisted of 155 healthy men and women volunteers (≥18 years of age) enrolled across four (4) external sites that are representative of the general population in the United States. The results are summarized in the table below.

Healthy Reference Range Intervals

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

N. INSTRUMENT

Quantra Hemostasis Analyzer (DEN180017)

O. SYSTEM DESCRIPTIONS

1. Modes of Operation:

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes __X__ or No _____

   Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

   Yes _____ or No __X__

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X__ or No _____

3. Specimen Identification:

   Bar code reader

4. Specimen Sampling and Handling:

   The QStat Cartridge requires a fresh sample of 3 mL or more of citrated whole blood collected in an evacuated tube containing 3.2% sodium citrate. The blood collection tube must be filled to the minimum fill line. The entire blood sample will be used for analysis on the Quantra. Do not use a discard tube as the sample as it may affect results or cause incomplete filling of the cartridge.

5. Calibration:

   User calibration is not required, based on the design of the instrument.

6. Quality Control:

   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 (with an accompanying package insert) for testing on the Quantra System. The controls are designed to be used as part of a laboratory quality control program and are manufactured with non-overlapping ranges for CT, CS, and FCS.

P. OTHER SUPPORTIVE INSTRUMENT PERFORMANCE CHARACTERISTICS DATA NOT COVERED IN THE "PERFORMANCE CHARACTERISTICS" SECTION

1. 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 including the following: a) anesthesiologists, b) surgeons, and c) other trained medical professionals who may assess the blood coagulation status of patients. 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.

Q. PROPOSED LABELING

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

R. CONCLUSION

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