



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

I Background Information:

A 510(k) Number

K232018

B Applicant

Haemonetics Corporation

C Proprietary and Established Names

Citrated: K, KH, RTH, FFH

D Regulatory Information

Product Code(s)		Regulation	
JPA	Class II	21 CFR 864.5425 - Multipurpose System For In Vitro Coagulation Studies	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

New assay

B Measurand:

Citrated Kaolin (CK), Citrated Kaolin with Heparinase (CKH), Citrated RapidTEG with Heparinase (CRTH), and Citrated Functional Fibrinogen with Heparinase (CFFH)

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 TEG 6s Hemostasis System consists of the TEG 6s Hemostasis Analyzer and the Citrated: K, KH, RTH, FFH assay cartridge. The TEG 6s Hemostasis System is intended for in vitro diagnostic use with adult patients where an evaluation of their blood hemostasis properties is desired. The TEG 6s Hemostasis System records the kinetic changes in a sample of 3.2% citrated whole blood as the sample clots and provides semi-quantitative results. The TEG 6s Hemostasis System can be used in the laboratory or at the point-of-care.

The Citrated: K, KH, RTH, FFH assay cartridge is intended to be used in patients where heparin/heparinoids may be present and who are at an increased risk of coagulopathy. Hemostasis evaluations are indicated to assess clinical conditions in cardiovascular surgery, cardiovascular procedures (e.g., minimally invasive valve replacement or repairs) and liver transplantation to assess hemorrhage or thrombosis conditions before, during and following the procedure.

The Citrated: K, KH, RTH, FFH assay cartridge contains four independent assays (CK, CKH, CRTH and CFFH) and the system output consists of a table of numerical values for parameters R, MA, and LY30.

The CK assay monitors the hemostasis process via the intrinsic pathway in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. Clotting characteristics are described by the functional parameters R (clotting time) and MA (maximum clot strength).

The CKH assay monitors the effects of heparin in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. CKH is used in conjunction with CK, and heparin influence is determined by comparing Clotting Times (R) between the two tests. LY30 describes fibrinolysis 30 minutes after reaching maximum clot strength.

The CRTH assay monitors the hemostasis process after stimulation of both the intrinsic and extrinsic pathways in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (maximum clot strength with contributions of both platelets and fibrin).

The CFFH assay monitors hemostasis of 3.2% citrated whole blood specimens in the TEG 6s Hemostasis System after blocking platelet contributions to clot strength, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (fibrinogen contribution to maximum clot strength).

Results from the TEG 6s analysis should not be the sole basis for a patient diagnosis, but should be evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests.

For professional use only.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

TEG 6s Hemostasis Analyzer

IV Device/System Characteristics:

A Device Description:

The TEG 6s Hemostasis System (TEG 6s Hemostasis Analyzer and the Citrated: K, KH, RTH, FFH assay cartridge) are used to test the hemostasis properties of citrated blood samples using four different assays/reagents simultaneously, one in each of the four cartridge channels. The TEG 6s Hemostasis System is designed to monitor and analyze the coagulation state of blood samples using thromboelastography technology. Thromboelastography has been utilized to understand the hemostatic balance that should exist between the extremes of coagulopathy (impaired clot formation, hypocoagulable) and thrombosis (formation of a blood clot obstructing the flow of blood, hypercoagulable). The TEG 6s analyzer records the kinetic changes in a whole blood sample as the sample clots, retracts and/or lyses. The system output consists of numerical values for each of the four cartridge channels resulting from the hemostasis process over time. For the CK assay, Kaolin-activated test methods are used to reduce variability and to reduce the running time of a native whole blood sample. CKH is similar to CK but with the addition of heparinase, to neutralize the effects of heparin in the blood. If there is heparin present, the R time for CK will be significantly longer than the R time for CKH. The CTRH assay neutralizes the anticoagulant property of heparin and maximally accelerates the clotting process by simultaneously activating the intrinsic and extrinsic coagulation pathways, allowing for the maximum clot strength to be reached more quickly. The CFFH assay neutralizes the anticoagulant property of heparin and inhibits platelet aggregation, excluding its contribution to clot strength, and thereby measures fibrinogen contribution to clot strength.

B Principle of Operation:

The TEG 6s technology is based on the use of Citrated K, KH, RTH, FFH disposable cartridge containing up to 4 independent measurement cells. Each cell consists of a short vertically oriented injection molded tube (ring). Detection of clotting in the TEG 6s Hemostasis System is performed optically. A piezoelectric actuator vibrates the measurement cell(s) through a motion profile composed of summed sinusoids at different frequencies. The movement of the measurement cells will induce motion in the sample meniscus, which will be detected by a photodiode. The resulting motion of the meniscus is monitored optically and analyzed by the instrument to calculate the resonant frequency and modulus of elasticity (stiffness) of the sample. By performing a Fast Fourier Transform (FFT) on meniscus motion data, the resonant frequencies can be determined. The analyzer monitors the harmonic motion of a hanging drop of blood in response to external vibration. As the sample transitions from a liquid state to a gel-like state during clotting, the modulus of elasticity (stiffness) and therefore resonant frequency

increase. The TEG 6s hemostasis analyzer measures these variations in resonant frequency during clotting and lysis.

Resonance is the tendency of a material or structure to oscillate with greater amplitude at some frequencies than others. The exact frequencies at which resonance occurs will depend on the stiffness and mass of the sample. Stiffness, in turn, is a function of a material's modulus of elasticity and the boundary conditions to which the material is exposed, such as the geometry and materials of a test cell. By holding these boundary conditions and sample mass constant from sample to sample, the TEG 6s Hemostasis System allows direct comparison of elasticity between samples. The output measurements are displayed in a table and on a graphical tracing that reflects the hemostasis profile of the clot formation.

In a typical test, blood that has been delivered to the measurement cell will not clot for several minutes. During this time the sample has no inherent stiffness except that provided by surface tension, and since this remains constant the measured resonant frequencies will not change. Once clotting begins, however, the elastic modulus and thus the resonant frequencies increase rapidly. During fibrinolysis, the process is reversed, with elastic modulus and resonant frequencies decreasing. In tests where clotting does not occur, the resonant frequency of the sample will not change. During coagulation, however, a clot will bind to the ring contained in the cartridge and the resonant frequency will rise with increasing firmness of the clot. The analyzer collects meniscus motion data, tracks changing resonant frequencies and analyzes the frequency data to provide semi-quantitative parameters describing the clot. The System monitors the interaction of platelets within the fibrin mesh of the clot during clot formation and lysis, all in a whole-blood setting. The TEG 6s Hemostasis System uses thromboelastography to provide continuous measurement of clot elasticity.

CK Principle

Kaolin is a standardized reagent consisting of dry Kaolin and 0.85% Saline solution. Kaolin-activated test methods are used to reduce variability and to reduce the running time of a native whole blood sample. Use of these particles of hydrated aluminum silicate shortens coagulation time because Kaolin acts as a contact surface activator (intrinsic pathway), which activates Factor XII and platelets and stimulates the reserve clotting ability of a blood sample. Kaolin is combined with CaCl_2 to neutralize any sodium citrate in the blood.

CKH Principle

Heparin is commonly used as an anticoagulant in surgical procedures. Even very low concentrations of heparin, fractions of IU/mL of blood, can noticeably increase the R time and can even completely anticoagulate the blood, making it difficult if not impossible to monitor developing coagulopathies that are masked by high levels of therapeutic heparin. The addition of heparinase in the assay cartridge neutralizes the effects of heparin in the sample. CaCl_2 is included to neutralize any sodium citrate in the blood.

CRT H Principle

RapidTEG maximally accelerates the clotting process by simultaneously activating the intrinsic and extrinsic coagulation pathways using a high concentration of Kaolin and Tissue Factor (TF). This closely reflects the physiological clotting process and yields results significantly faster than a native, Kaolin, and/or TF activated test. The addition of heparinase in the assay cartridge neutralizes the effects of heparin in the sample. CaCl_2 is included to neutralize any sodium citrate in the blood.

CFFH Principle

The Functional Fibrinogen reagent activates the extrinsic pathway using tissue factor and inhibits platelet aggregation using a platelet inhibitor that binds to GPIIb/IIIa receptors. By excluding the platelet aggregation contribution to clot strength (MA), the reagent measures fibrinogen contribution. The addition of heparinase in the assay cartridge neutralizes the effects of heparin in the sample. Functional Fibrinogen is combined with CaCl₂ to neutralize any sodium citrate in the blood. Determining the independent contribution of platelets and fibrinogen further improves the use of the TEG 6s System in helping to detect and diagnose hemostasis defects.

V Substantial Equivalence Information:

A Predicate Device Name(s):

TEG 6s with the Citrated Multichannel Cartridge

B Predicate 510(k) Number(s):

K150041

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K232018</u>	<u>K150041</u>
Device Trade Name	Citrated: K, KH, RTH, FFH	TEG 6s with the Citrated Multichannel Cartridge
General Device Characteristic Similarities		
Intended Use/Indications For Use	The TEG 6s Hemostasis System consists of the TEG 6s Hemostasis Analyzer and the Citrated: K, KH, RTH, FFH assay cartridge. The TEG 6s Hemostasis System is intended for in vitro diagnostic use with adult patients where an evaluation of their blood hemostasis properties is desired. The TEG 6s Hemostasis System records the kinetic changes in a sample of 3.2% citrated whole blood as the sample clots and provides semi-quantitative results. The TEG 6s Hemostasis System can be used in the laboratory or at the point-of-care.	The TEG 6s Hemostasis System is intended for in vitro diagnostic use to provide semiquantitative indications of the hemostasis state of a blood sample. The Citrated Multichannel Cartridge, to be used with the TEG 6s analyzer, contains four independent assays (CK, CRT, CKH and CFF), described below. The CK assay monitors the hemostasis process via the intrinsic pathway in 3.2% citrated whole blood specimens on the TEG 6s System. Clotting

	The Citrated: K, KH, RTH, FFH assay cartridge is intended to be used in patients where heparin/heparinoids may be present and who are at an increased risk of coagulopathy. Hemostasis evaluations are indicated to assess clinical conditions in cardiovascular surgery, cardiovascular procedures (e.g., minimally invasive valve replacement or repairs) and liver transplantation to assess hemorrhage or thrombosis conditions before, during and following the procedure. The Citrated: K, KH, RTH, FFH assay cartridge contains four independent assays (CK, CKH, CPTH and CFFH) and the system output consists of a table of numerical values for parameters R, MA, and LY30. The CK assay monitors the hemostasis process via the intrinsic pathway in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. Clotting characteristics are described by the functional parameters R (clotting time) and MA (maximum clot strength). The CKH assay monitors the effects of heparin in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. CKH is used in conjunction with CK, and heparin influence is determined by comparing Clotting Times (R) between the two tests. LY30 describes fibrinolysis 30 minutes after reaching maximum clot strength.	characteristics are described by the functional parameters Clotting Time (R), Speed of Clot Formation (K and Alpha angle) and Maximum Clot Strength (MA). The CRT assay monitors the hemostasis process via both the intrinsic and extrinsic pathways in 3.2% citrated whole blood specimens on the TEG 6s System. Clotting characteristics are described by the functional parameter Maximum Clot Strength (MA). The CRT MA parameter is equivalent to the CK MA parameter but the final MA value is reached more quickly using the CRT assay. The CKH assay monitors the effects of heparin in 3.2% citrated whole blood specimens on the TEG 6s System. CKH is used in conjunction with CK, and heparin influence is determined by comparing Clotting Times (R) between the two tests. The CFF assay monitors hemostasis of 3.2% citrated whole blood specimens in the TEG 6s System after blocking platelet contributions to clot strength. Clotting characteristics are described by the functional parameters Maximum Clot Strength (MA) and the Estimated Functional Fibrinogen Level (FLEV). Results from the TEG 6s analysis should not be the sole basis for a patient diagnosis, but should be
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	The CRTH assay monitors the hemostasis process after stimulation of both the intrinsic and extrinsic pathways in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (maximum clot strength with contributions of both platelets and fibrin). The CFFH assay monitors hemostasis of 3.2% citrated whole blood specimens in the TEG 6s Hemostasis System after blocking platelet contributions to clot strength, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (fibrinogen contribution to maximum clot strength). Results from the TEG 6s analysis should not be the sole basis for a patient diagnosis, but should be evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests. For professional use only.	evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests. The indication for TEG 6s System use is with adult patients where an evaluation of their blood hemostasis properties is desired. Hemostasis evaluations are commonly used to assess clinical conditions in cardiovascular surgery and cardiology procedures to assess hemorrhage or thrombosis conditions before, during and following the procedure.
Measurement Principle	Changes in physical clot elasticity over time; monitoring the physical response of a clot to low levels of applied strain (resonance frequency)	Same
Sample Matrix	3.2% citrated whole blood	Same
Measurement Output	Graphical tracings of resonant frequency per reagent type, table of parameters	Same

Assays	CK CKH	Same
Assay Reagents	CK – kaolin and CaCl ₂ CKH – kaolin and CaCl ₂ with heparinase	Same
Measuring Chambers	4	Same
Sample Volume (per chamber)	20 µL	Same
Quality Control	Cartridge Reagent QC - Level 1 Cartridge Reagent QC - Level 2	Same
General Device Characteristic Differences		
Assay Reagents	CRT – tissue factor, kaolin and CaCl ₂ with heparinase CFFH – abciximab, tissue factor and CaCl ₂ with heparinase	CRT – tissue factor, kaolin and CaCl ₂ CFF – abciximab, tissue factor and CaCl ₂
Assay Parameters Reported	CK: R, MA CKH: R, LY30 CRT: MA CFFH: MA	CK: R, K, Angle, MA CKH: R CRT: MA CFF: MA, FLEV

VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3: *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline* - Third Edition
- CLSI EP28-A3c: *Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline* - Third Edition
- CLSI EP07-A3: *Interference Testing in Clinical Chemistry* - 3rd Edition
- CLSI EP25-A *Evaluation of Stability of In Vitro Diagnostic Reagents: Diagnostic Reagents; Approved Guideline*
- CLSI EP17-A2: *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline* -Second Edition
- IEC 61010-1:2010: Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements
- IEC 61010-2-010: 2019: Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-010: Particular requirements for laboratory equipment for the heating of materials
- IEC 61010-2-101: 2018: Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment
- IEC 60601-1-2:2014/AMD1: 2020: Amendment 1 - Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests

- IEC/ EN61326-1: 2020: Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 1: General requirements
- IEC/ EN61326-2-6: 2020: Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 2-6: Particular requirements - In vitro diagnostic (IVD) medical equipment

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Repeatability – 20-day precision:

A precision study was conducted based on the CLSI EP05-A3 guideline for an assessment of the Citrated: K, KH, RTH, FFH assay cartridge repeatability utilizing the TEG 6s Cartridge Reagent Quality Control (QC) material. Two levels of QC material were tested (Level 1 and 2) with a single lot of Citrated: K, KH, RTH, FFH assay cartridges at a single site with two TEG 6s hemostasis analyzers (one analyzer per QC Level). One trained operator performed two runs per day with two replicates per run for 20 days. To demonstrate precision performance for both levels of QC, the mean, standard deviation (SD) and coefficient of variation (%CV) for each component of variability were calculated including repeatability, between-run, between-day, and within laboratory. The determination of acceptability was based on the SD or %CV.

20-day Precision – QC Level 1										
			Repeatability		Between Run		Between Day		Within Laboratory	
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK-R (min)	80	6.10	0.54	8.9	0.00	0.0	0.27	4.4	0.61	10.0
CKH-R (min)	80	4.46	0.30	6.7	0.09	2.0	0.10	2.3	0.33	7.3
CK-MA (mm)	80	67.04	0.93	1.4	0.00	0.0	0.48	0.7	1.04	1.6
CRT-MA (mm)	80	58.37	1.18	2.0	0.00	0.0	0.95	1.6	1.52	2.6
CFFH-MA (mm)	80	63.31	1.35	2.1	0.00	0.0	1.05	1.6	1.71	2.7
CKH LY30 (%)	80	Data not collected								

20-day Precision – QC Level 2										
			Repeatability		Between Run		Between Day		Within Laboratory	
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK-R (min)	80	1.24	0.07	5.8	0.05	3.6	0.00	0.0	0.09	6.9
CKH-R (min)	80	1.25	0.08	6.1	0.02	1.5	0.00	0.0	0.08	6.3
CK-MA (mm)	79*	26.71	1.21	4.5	0.00	0.0	0.84	3.1	1.47	5.5
CRT-MA (mm)	80	27.69	1.29	4.7	0.00	0.0	0.89	3.2	1.57	5.7
CFFH-MA (mm)	80	27.83	1.26	4.5	0.00	0.0	0.91	3.3	1.55	5.6
CKH LY30 (%)	80	92.26	0.40	0.4	0.40	0.4	0.00	0.0	0.56	0.6

*1 outlier removed

Lot-to-Lot Precision Study

A lot-to-lot precision study was performed at one internal site using three lots of Citrated: K, KH, RTH, FFH assay cartridges and two lots of Cartridge Reagent QC Level 1 and Level 2. Testing was performed by two trained operators using six different TEG 6s hemostasis analyzers over 10 days. To demonstrate precision performance for both levels of QC, the mean, SD and %CV for each component of variability were calculated including repeatability, between-day, between-operator, between-QC Lot, between-Cartridge Lot, and within-laboratory. The determination of acceptability was based on the SD or %CV.

Lot-to-Lot Precision – QC Level 1														
Assay-Parameter	N	Mean	Repeatability		Between Day		Between Operator		Between QC Lot		Between Cartridge Lot		Within Laboratory	
			SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
CK-R (min)	120	6.22	0.50	8.1	0.11	1.7	0.00	0.0	0.12	2.0	0.02	0.4	0.53	8.5
CKH-R (min)	120	4.76	0.41	8.5	0.12	2.6	0.00	0.0	0.25	5.2	0.12	2.5	0.50	10.6
CK-MA (mm)	120	66.62	1.57	2.4	0.14	0.2	0.00	0.0	1.37	2.1	0.00	0.0	2.09	3.1
CRTH-MA (mm)	120	59.68	1.81	3.0	0.35	0.6	0.11	0.2	0.00	0.0	0.00	0.0	1.85	3.1
CFFH-MA (mm)	120	64.12	1.05	1.6	0.00	0.0	0.20	0.3	0.00	0.0	0.61	1.0	1.23	1.9
CKH LY30 (%)	Data not collected													

Lot-to-Lot Precision – QC Level 2														
Assay-Parameter	N	Mean	Repeatability		Between Day		Between Operator		Between QC Lot		Between Cartridge Lot		Within Laboratory	
			SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
CK-R (min)	120	1.16	0.06	5.1	0.02	1.4	0.03	2.7	0.06	5.0	0.01	0.7	0.09	7.7
CKH-R (min)	120	1.15	0.05	4.8	0.02	1.3	0.03	2.8	0.07	5.7	0.00	0.0	0.09	8.1
CK-MA (mm)	118*	28.02	1.51	5.4	0.26	0.9	0.47	1.7	0.72	2.6	0.23	0.8	1.78	6.3
CRTH-MA (mm)	120	29.40	1.52	5.2	0.74	2.5	0.81	2.8	0.83	2.8	0.30	1.0	2.07	7.0
CFFH-MA (mm)	120	28.84	1.08	3.8	0.32	1.1	0.68	2.4	0.95	3.3	0.13	0.5	1.63	5.7
CKH LY30 (%)	120	92.68	0.36	0.4	0.00	0.0	0.00	0.0	0.10	0.1	0.04	0.1	0.37	0.4

* Two outliers removed

Reproducibility

A reproducibility study was conducted at three sites (two external and one internal) utilizing one lot of TEG 6s Cartridge Reagent QC material. Two levels of QC material were tested (Level 1 and 2) with a single lot of Citrated: K, KH, RTH, FFH assay cartridges by one operator each site per day over a period of five days with five replicates per QC Level per

day. To demonstrate precision performance for both levels of QC, the mean, SD and %CV for each component of variability were calculated including repeatability, between-day, between-site (includes operators and analyzer variation) and reproducibility. The determination of acceptability was based on the SD or %CV.

Reproducibility – QC Level 1										
			Repeatability		Between Day		Between Site*		Reproducibility	
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK-R (min)	75	6.18	0.40	6.4	0.04	0.6	0.39	6.3	0.56	9.0
CKH-R (min)	75	4.62	0.33	7.2	0.09	1.9	0.26	5.7	0.43	9.4
CK-MA (mm)	75	66.06	1.33	2.0	0.00	0.0	0.56	0.8	1.44	2.2
CRTH-MA (mm)	75	60.34	1.52	2.5	0.37	0.6	1.76	2.9	2.36	3.9
CFFH-MA (mm)	75	63.97	1.03	1.6	0.00	0.0	2.11	3.3	2.34	3.7
CKH LY30 (%)	75	Data not collected								

*Between site includes operator and analyzer variation.

Reproducibility – QC Level 2										
			Repeatability		Between Day		Between Site*		Reproducibility	
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK-R (min)	75	1.13	0.22	0.2	0.12	0.1	0.00	0.0	0.25	0.3
CKH-R (min)	75	1.13	0.05	4.7	0.00	0.0	0.01	1.1	0.05	4.8
CK-MA (mm)	75	28.18	0.77	2.8	0.24	0.8	0.51	1.8	0.96	3.4
CRTH-MA (mm)	75	30.20	1.12	3.7	0.44	1.5	0.38	1.3	1.26	4.2
CFFH-MA (mm)	75	29.53	0.81	2.7	0.31	0.1	0.27	0.9	0.91	3.1
CKH LY30 (%)	75	92.30	0.22	0.2	0.12	0.1	0.00	0.0	0.25	0.3

*Between site includes operator and analyzer variation.

Whole Blood Repeatability

A whole blood repeatability study was conducted using whole blood samples under the following conditions: normal, contrived hypocoagulable (low CFFH MA, low CRTH MA), hypercoagulable (high CRTH MA and High CKH LY30) and hyperfibrinolytic (High CKH LY30). All sample conditions were analyzed by two trained operators using three lots of Citrated: K, KH, RTH, FFH assay cartridges with two replicates per run. Normal whole blood samples were tested in one day with two operators testing three cartridge lots on two different TEG 6s hemostasis analyzers with two replicates per run (n=24). Due to sample stability limitations for contrived samples (hypocoagulable, hypercoagulable, and hyperfibrinolytic), testing was completed in one day by two operators using three cartridge lots on four analyzers for one replicate (n=24). To demonstrate precision performance for all sample types, the mean, SD and %CV for each component of variability were calculated including repeatability, between-operator, between-lot, between device (normal sample type only), and within-laboratory. The determination of acceptability was based on the SD or %CV.

Whole Blood Repeatability – Normal Sample												
			Repeatability		Between Operator		Between Lot		Between Device/Day		Within Laboratory	
Assay-Parameter	N	Mean	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
CK-R (min)	24	7.50	0.4	5.9	0.00	0.0	0.65	8.7	0.28	3.8	0.83	11.2
CKH-R (min)	24	7.60	0.75	10.0	0.00	0.0	0.00	0.0	0.14	1.8	0.77	10.1
CK-MA (mm)	24	54.80	0.96	1.7	0.32	0.6	0.54	1.0	0.25	0.5	1.17	2.1
CRTH-MA (mm)	24	17.00	0.27	1.6	0.46	2.7	0.09	0.6	0.60	3.5	0.81	4.8
CFFH-MA (mm)	24	57.00	1.43	2.5	0.65	1.1	0.20	0.4	0.00	0.0	1.58	2.8
CKH LY30 (%)	24	0.30	0.13	51.0	0.00	0.0	0.10	36.5	0.08	32.1	0.18	70.4

Whole Blood Repeatability – Hypocoagulable (Sample 2)											
Citratd whole blood was spiked with Abciximab and Dabigatran											
			Repeatability*		Between Operator		Between Lot		Within Laboratory		
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	
CK-R (min)	24	13.29	1.47	11.01	0.00	0.0	0.00	0.0	1.47	11.1	
CKH-R (min)	24	13.09	1.52	11.6	0.61	4.6	0.39	3.0	1.68	12.8	
CK-MA (mm)	24	52.78	1.04	2.0	0.00	0.0	0.89	1.7	1.37	2.6	
CRTH-MA (mm)	24	58.55	0.51	0.9	0.00	0.0	0.35	0.6	0.62	1.1	
CFFH-MA (mm)	24	18.02	0.17	1.0	0.03	0.2	0.12	0.7	0.21	1.2	
CKH LY30 (%)	24	1.18	0.19	16.1	0.00	0.0	0.00	0.0	0.19	16.1	

* Repeatability includes between analyzer variance.

Whole Blood Repeatability – Hypocoagulable (Sample 3)											
Citratd Whole blood sample was diluted to 50% fibrinogen with fibrinogen deficient plasma.											
			Repeatability*		Between Operator		Between Lot		Within Laboratory		
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	
CK-R (min)	24	4.91	0.31	6.3	0.03	0.7	0.12	2.4	0.33	6.8	
CKH-R (min)	24	4.85	0.20	4.2	0.00	0.0	0.11	2.4	0.23	4.8	
CK-MA (mm)	24	44.71	0.69	1.6	0.49	1.1	0.39	0.9	0.94	2.1	
CRTH-MA (mm)	24	43.69	0.83	1.9	0.00	0.0	0.00	0.0	1.19	2.7	
CFFH-MA (mm)	24	10.18	0.83	8.1	0.20	2.3	0.30	3.3	0.92	9.2	
CKH LY30 (%)	24	Data not collected									

Whole Blood Repeatability – Hypercoagulable (Sample 4)											
Citratd whole blood sample was collected and prepared using platelet rich plasma (PRP) and concentrated fibrinogen.											
			Repeatability*		Between Operator		Between Lot		Within Laboratory		
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	
CK-R (min)	23*	5.47	0.61	10.7	0.37	6.5	0.05	0.8	0.71	12.5	
CKH-R (min)	23*	5.91	0.72	12.2	0.00	0.0	0.46	7.8	0.85	14.5	
CK-MA (mm)	23*	70.69	0.35	0.5	0.27	0.4	0.27	0.4	0.51	0.7	
CRTH-MA (mm)	24	71.59	0.39	0.5	0.00	0.0	0.00	0.0	0.39	0.5	
CFFH-MA (mm)	24	51.38	0.92	1.8	0.18	1.5	2.81	5.5	3.06	6.0	
CKH LY30 (%)	24	Data not collected									

*One outlier removed

Whole Blood Repeatability – Hypercoagulable (Sample 5)										
Citratd whole blood was spiked with Fibrinogen using cryo-precipitate										
			Repeatability*		Between Operator		Between Lot		Within Laboratory	
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK-R (min)	24	6.60	0.51	7.7	0.10	1.5	0.24	3.6	0.57	8.6
CKH-R (min)	24	6.28	0.66	10.6	0.00	0.0	0.24	3.8	0.71	11.2
CK-MA (mm)	24	63.85	0.75	1.2	0.00	0.0	0.19	0.3	0.77	1.2
CRTH-MA (mm)	24	66.59	0.26	0.4	0.00	0.0	0.13	0.2	0.29	0.4
CFFH-MA (mm)	24	32.92	0.66	2.0	0.00	0.0	0.53	1.6	0.85	2.6
CKH LY30 (%)	24	0.45	0.44	97.1	0.00	0.0	0.14	31.0	0.46	101.9

* Repeatability includes between analyzer variance.

Whole Blood Repeatability – Hyperfibrinolytic (Sample 6)										
Whole blood was spiked with tPA (tissue factor)										
			Repeatability*		Between Operator		Between Lot		Within Laboratory	
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK-R (min)	24	6.38	0.45	7.1	0.00	0.0	0.51	8.0	0.68	10.7
CKH-R (min)	24	6.53	0.54	8.3	0.00	0.0	0.00	0.0	0.54	8.3
CK-MA (mm)	24	58.69	0.96	1.6	0.00	0.0	0.10	0.2	0.96	1.6
CRTH-MA (mm)	24	61.56	0.68	1.1	0.38	0.6	0.00	0.0	0.78	1.3
CFFH-MA (mm)	24	21.70	1.01	4.6	0.28	1.3	1.25	5.7	1.63	7.5
CKH LY30 (%)	24	15.87	1.59	9.7	0.00	0.0	0.00	0.0	1.59	9.7

* Repeatability includes between analyzer variance.

Whole Blood Repeatability – Hypercoagulable (Sample 7)										
Citratd whole blood sample was spiked with diluted tissue factor										
			Repeatability*		Between Operator		Between Lot		Within Laboratory	
Assay-Parameter	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK-R (min)	24	4.41	0.17	3.8	0.00	0.0	0.13	2.9	0.21	4.8
CKH-R (min)	24	4.31	0.19	4.3	0.00	0.0	0.08	1.9	0.20	4.7
CK-MA (mm)	24	64.38	0.44	0.7	0.11	0.2	0.28	0.4	0.54	0.8
CRTH-MA (mm)	24	65.65	0.40	0.6	0.16	0.2	0.00	0.0	0.43	0.6
CFFH-MA (mm)	24	25.18	0.43	1.7	0.17	0.7	0.52	2.1	0.69	2.7
CKH LY30 (%)	24	0.67	0.15	23.1	0.03	4.2	0.13	20.0	0.21	30.8

* Repeatability includes between analyzer variance.

2. Linearity:

Not applicable.

3. Analytical Specificity/Interference:

Interference testing was conducted using Citratd: K, KH, RTH, FFH assay cartridge with 3.2% sodium citrated whole blood in accordance with CLSI EP07-A3. The study included 13 potential interferents and the impact of four potential interferent factors: lack of discard tube, excess hemolysis, hemodilution, and short draw. Each potential interferent or interferent factor was evaluated in three replicates on normal, hyperfibrinolytic, and

hypocoagulable conditions. A control sample was tested with each condition in which the blood was not treated with the potential interferent or interferent factor.

The following interfering substances were evaluated and showed no significant interference up to the specified concentration in whole blood samples collected in 3.2% sodium citrate anticoagulant collection tubes.

Interferent	Highest Concentration with No Interference
Endogenous Substances	
lipemia	300 mg/dL
Exogenous Substances	
alcohol	320 mg/dL
ticagrelor	1.8 µg/mL
tranexamic acid (TXA)	200 µg/mL
epsilon aminocaproic acid (EACA)	600 µg/mL
Mycophenolic Acid	42 µg/mL
Tacrolimus	144 ng/mL
Prednisone	99 ng/mL
Rifaximin	40.5 ng/mL
Lactulose	12 µg/mL
Aspirin	Normal – 6.5 mg/dL Hyperfibrinolytic – 6.5 mg/dL (CK-R, CK-MA, CKH-R, CRTH-MA, CFFH-MA) 0 mg/dL (CKH-LY30)
Dabigatran	Normal – 0 ng/mL (CK-R, CKH-R), 90 ng/mL (CKH-LY30), 180 ng/mL (CK-MA, CRTH-MA, CFFH-MA) Hyperfibrinolytic – 0 ng/mL (CK-R, CKH-R, CKH-LY30), 90 ng/mL (CK-MA), 180 ng/mL (CRTH-MA, CFFH-MA)
Rivaroxaban	Normal – 50 ng/mL (CK-R, CKH-R) 400 ng/mL (CK-MA, CKH-LY30, CRTH-MA, CFFH-MA) Hyperfibrinolytic – 50 ng/mL (CK-R, CKH-R), 200 ng/mL (CK-MA), 400 ng/mL (CKH-LY30, CRTH-MA, CFFH-MA)

Interferent Factors	Specimen Condition	Highest Concentration with No Interference
No Discard Tube	Normal	No interference
	Hypocoagulable	No interference
	Hyperfibrinolytic	CKH-LY30
Hemolysis	Normal	CK-R, CK-MA, CKH-R, CRTH-MA, CFFH-MA – 400 mg/dl CKH-LY30 – 200 mg/dL
	Hypocoagulable	All parameters – 400 mg/dl
	Hyperfibrinolytic	CK-R, CK-MA, CFFH-MA – 400 mg/dl CKH-R – 200 mg/dL CRTH-MA – 100 mg/dL CKH-LY30 – 0 mg/dL
Hemodilution	Normal	CK-R, CK-MA, CKH-R, CKH-LY30 – 50% CRTH-MA – 20% CFFH-MA – 40%

Interferent Factors	Specimen Condition	Highest Concentration with No Interference
	Hypocoagulable	CK-R, CKH-R, CKH-LY30 – 50% CK-MA, CRTH-MA – 0% CFFH-MA – 40%
	Hyperfibrinolytic	CK-R, CKH-R – 50% CK-MA, CKH-LY30, CRTH-MA – 0% CFFH-MA – 20%
Short Draw	Normal	CK-R, CK-MA, CKH-R, CKH-LY30, CFFH-MA – 60% CRTH-MA – 70%
	Hypocoagulable	CK-R, CK-MA, CKH-LY30, CRTH-MA, CFFH-MA – 60% CKH-MA – 70%
	Hyperfibrinolytic	CK-R, CK-MA, KH-R, CRTH-MA, CFFH-MA – 60% CKH-LY30 – 70%

4. Assay Reportable Range:

Validation that the Citrated: K, KH, RTH, FFH assay cartridge parameters demonstrate functional performance across the claimed reportable ranges for each parameter was supported by data from the clinical validation study.

Parameter	Reportable Range
CK-R (min)	0.4–17
CK-MA (mm)	40–75
CKH-R (min)	0.3–17
CRTH-MA (mm)	20–78
CFFH-MA (mm)	6–61
CKH-LY30 (%)	0–30

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

Shelf-Life Stability Study

To establish the shelf-life stability of the Citrated: K, KH, RTH, FFH assay cartridge, a real-time stability study is designed following CLSI EP25-A. The shelf-life stability study includes three cartridge lots stored at 2–8°C and cartridges are taken out for evaluation at 0, 12, 18, 24 and 26.5 months. Cartridges are tested using 3.2% sodium citrate samples using 16 cartridges at each sample condition. Sample conditions include unspiked donor whole blood and donor whole blood spiked with 5 IU/mL Heparin. The cartridges were tested at time zero (T0) and lot one was tested after the transport stability study (day 93). Cartridge stability will be assessed through regression analysis of the individual value difference from T0 compared to each sample type and assay parameter in accordance with CLSI EP25-A. Shelf-life cartridge stability studies are on-going.

Transport Stability Study

The transport simulation study was performed with one lot of Citrated: K, KH, RTH, FFH assay cartridge to simulate transport under stressed conditions. To create the stressed condition, cartridges were exposed to an extended seven-day International Safe Transit Association (ISTA) 7-day shipping conditions (5°C for 24 hours (Preconditioning), 22°C for 4 hours, 35°C for 6 hours, 30°C for 152 hours, and 35°C for 6 hours). The measured drift for

each testing time point and condition was compared to the mean level obtained at T0 (time 0). All results were within the acceptable allowable drift. The cartridges passed transport stability testing and demonstrate the cartridges are robust. The one lot of cartridges used in the Shelf-Life Stability Study and Cartridge In-Use Stability Study were the lot tested in the Transport Stability Study to demonstrate the real-world use scenario.

Cartridge In-Use Stability Study

To support a 2 hour in-use stability of the Citrated: K, KH, RTH, FFH assay cartridge, three lots of cartridges were tested at T0 and 2.5 hours after removal from packaging. Sodium citrated whole blood collected from normal donors were tested on 10 cartridges and 1 IU/mL Heparin Spiked Blood and 7 IU/mL Heparin Spiked Blood were tested on 18 cartridges each. The results from each assay were compared to the control measurements at T0. The data support the cartridge can be stable after removal from the sealed cartridge pouch for up to 2 hours at ambient room temperature (20–22°C) and humidity (<50%).

Whole Blood Sample Stability Study

A whole blood sample stability study was conducted to support the stability of whole blood samples collected in 3.2% sodium citrate tubes after 10 minutes of incubation and up to 2 hours of storage at ambient room temperature (20–22°C). Samples were tested at T0 (as soon as practical post draw), 10 (incubation time point prior to assay start), 66, 99, and 132 minutes. A total of six donor samples per sample type were tested in six replicates per time point. The sample types used included normal, hypocoagulable, hypercoagulable, and hyperfibrinolytic whole blood. Replicates were executed simultaneously using six TEG 6s hemostasis Analyzers. All Citrated: K, KH, RTH, FFH reported parameters (CK-R, CK-MA, CKH-R, CKH-LY30, CRTH-MA, and CFFH-MA) were evaluated. Results of the study support the use of whole blood collected in 3.2% sodium citrate tubes up to two hours after collection and following a 10-minute incubation after collection.

6. Detection Limit:

Not applicable.

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The method comparison study was performed at eight clinical sites in the United States, comparing to the TEG 6s hemostasis analyzers with the Citrated Multichannel Cartridge (K150041) and STA - Fibrinogen 5 (K840211). The study enrolled 338 patients (145 females and 192 males), 18 years of age or older who are at an increased risk of coagulopathy. Enrolled subjects were patients undergoing liver transplantation, cardiovascular surgery, or cardiology procedures. Blood samples were drawn before, during, and after the procedures and analyzed by 24 trained operators.

To support the use of the CKH-MA and CKH-LY30 parameters in the Citrated Multichannel Cartridge (K150041), additional analytical validation studies were performed. The results of

the method comparison study comparing the candidate device, Citrated: K, KH, RTH, FFH assay cartridge to the predicate, Citrated Multichannel Cartridge (K150041) and STA - Fibrinogen 5 (K840211) demonstrate substantial equivalence for all reportable parameters.

Parameter	N	Intercept [95% CI]	Slope [95% CI]	Pearson Coefficient [95% CI]
CK-R	617	-0.45 [-0.769; -0.125]	1.08 [1.041; 1.126]	0.90 [0.878; 0.910]
CK - MA	539	-3.43 [-5.127; -1.731]	1.05 [1.022; 1.082]	0.95 [0.939; 0.956]
CKH - R	829	-0.17 [-0.538; 0.193]	1.01 [0.960; 1.055]	0.82 [0.800; 0.844]
CKH - LY30	828	-0.01 [-0.095; 0.071]	1.00 [0.988; 1.010]	0.99 [0.985; 0.989]
CRTN - MA	870	-5.54 [-6.4626; -4.459]	1.11 [1.094; 1.133]	0.97 [0.962; 0.910]
CFFH - MA *	883	-78.71 [-98.9; -58.53]	1.32 [1.25; 1.40]	--

*Claus Fibrinogen comparator

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

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

CK Sensitivity and Specificity:

To define the sensitivity and specificity for the CK channel, blood samples were collected from four normal donors to establish hypocoagulable, hypercoagulable and hyperfibrinolytic conditions. Four Levels – including baseline of citrated whole blood samples spiked with increasing concentration of heparin (0, 0.1, 0.15, and 0.20 IU/mL) were tested with five TEG 6s Citrated: K, KH, RTH, FFH assay cartridges for a total of 20 cartridges per run.

All hypo-coagulable, hyper-coagulable and hyper-fibrinolytic samples without heparin showed 100% specificity and all samples spiked at 0.2 IU/ml showed 100% sensitivity for the detection of heparin.

Heparin Neutralization Requirement Verification

A study was performed to validate the use of heparinase to neutralize the effect of heparin in blood samples. Tests were performed using Unfractionated Heparin (UFH) and Low Molecular Weight Heparin (LMWH) spiked samples and un-spiked samples. A total of 200 cartridges were tested across whole blood samples collected in 3.2% sodium citrate tubes from four donors in 10 replicates. The mean result per test specimen condition fell within the respective normal reference range for CRTH-MA, CFFH-MA, CKH-R, and CKH-LY30 for all donors. The study verified the defined heparin neutralization performance requirements:

- The CKH, CRTH, and CFFH assays shall be able to neutralize up to 5.0 IU/mL (+/- 0.1IU/mL) of heparin.
- The CKH, CRTH, and CFFH assays shall be able to neutralize up to 0.013 mg/mL (+/- 0.001 mg/mL) of LMWH.

The tolerance interval (95% confidence for 90% of the population) calculated for CFFH-MA, and CRTH-MA for all specimen types fell within the respective normal reference range. The study acceptance criteria were met and has verified the following heparin neutralization performance requirements:

- Blood treated with 5.0 IU/ml (+/- 0.1IU/mL) of heparin, measured CFFH-MA, shall remain within the normal reference range, 90% of the time.
- Blood treated with 5.0 IU/ml (+/- 0.1IU/mL), measured CRTH-MA, shall remain within the normal reference range, 90% of the time.

For all 0.008 mg/mL LMWH contrived samples, the CK-R value was greater than the CKH-R value. The study acceptance criteria were met and has verified the following heparin neutralization performance requirement for the LMWH sample condition:

- CK-R shall be greater than CKH-R when at least 0.2 IU/mL of heparin or at least 0.008 mg/mL LMWH is present in the blood sample.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

The reference ranges for the Citrated: K, KH, RTH, FFH assay cartridge parameters were established according to CLSI EP28-A3c. The study included 164 apparently healthy individuals (84 males and 80 female), greater than 18 years old with no known coagulopathies and not taking any drugs that would potentially affect patient hemostasis. The non-parametric method for analysis was used to determine the reference range for each assay parameter. The following table contains the reference range data for each parameter.

Parameter	N	Range
CK-R (min)	157	4.6–9.1
CK-MA (mm)	151	52–69
CKH-R (min)	155	4.3–8.3
CKH-LY30 (%)	148	0–3.2

Parameter	N	Range
CRTH-MA (mm)	162	53–69
CFFH-MA (mm)	162	15–34

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.