May 9, 2019

Haemonetics Corporation
Mark Anzalone
Manager, Regulatory Affairs
400 Wood Road
Braintree, Massachusetts 02184

Re: K183160
Trade/Device Name: TEG 6s Hemostasis System
Regulation Number: 21 CFR 864.5425
Regulation Name: Multipurpose system for in vitro coagulation studies
Regulatory Class: Class II
Product Code: JPA
Dated: November 14, 2018
Received: November 15, 2018

Dear Mark Anzalone:

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 electronic 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

For

Lea Carrington
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K183160

Device Name
TEG® 6s Hemostasis System

Indications for Use *(Describe)*
The TEG® 6s Hemostasis System consists of the TEG 6s Hemostasis Analyzer and TEG 6s Citrated: K, RT, FF Assay Cartridge. The TEG 6s Hemostasis System is intended for in vitro diagnostic use to provide semi-quantitative indications of the hemostasis state of a venous blood sample. The TEG 6s Hemostasis System records the kinetic changes in a sample of 3.2% citrated whole blood as the sample clots.

The Citrated: K, RT, FF Assay Cartridge contains three independent assays (CK, CRT and CFF) and the system output consists of a table of numerical values for parameters R, LY30, and MA.

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 LY30 (fibrinolysis after 30 minutes of reaching maximum clot strength).

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 Hemostasis System. Clotting characteristics are described by the functional parameter MA (maximum clot strength).

The CFF assay monitors hemostasis of 3.2% citrated whole blood specimens in the TEG 6s Hemostasis System after blocking platelet contributions to clot strength. Clotting characteristics are described by the functional parameter MA (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. The indication for TEG 6s Hemostasis System use is with adult patients (18 years and older) where an evaluation of their blood hemostasis properties is desired. Hemostasis evaluation with the TEG 6s Hemostasis System using the Citrated: K, RT, FF Assay Cartridge is used to assess clinical conditions in a trauma setting to assess hemorrhage or thrombosis conditions.

For professional 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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

HAEMONETICS®

510(k) Summary

Date: April 8, 2019

SUBMITTER

Haemonetics Corporation
400 Wood Road
Braintree, MA 02184

CONTACT

Mark Anzalone
Manager, Regulatory Affairs
Phone: 781-356-9912
Fax: 781-356-3558
Email: mark.anzalone@haemonetics.com

DEVICE INFORMATION

Trade Name:	TEG® 6s Hemostasis System / TEG® 6s Citrated: K, RT, FF Assay Cartridge
Common Name:	Whole Blood Hemostasis System
Classification Name:	Multipurpose System for *in vitro* Coagulation Studies
Regulation Number:	21 CFR 864.5425
Product Code:	JPA, GGN
Device Class:	2

PREDICATE DEVICE

Thrombelastograph® Coagulation Analyzer (TEG®) – 5000, K993678/K002177, Product Code JPA (System, Multipurpose, for In Vitro Coagulation Studies), Haemoscope Corporation

DESCRIPTION OF THE DEVICE

System Description

The TEG® 6s Hemostasis System (TEG® Hemostasis analyzer and TEG® 6s Assay Cartridges) is intended for in vitro diagnostic use to provide semi-quantitative indications of a blood sample's ability to form and maintain a clot. The TEG® 6s Hemostasis System records the kinetic changes in a sample of whole blood as the sample clots, retracts and/or lyses. The system output consists of a table of numerical values resulting from the hemostasis process over time. This information can be used by clinicians to aid in determining if a dysfunction or coagulopathy is present.

To perform a test, a disposable TEG® 6s Assay Cartridge is inserted into the TEG® 6s Hemostasis analyzer. The instrument reads the bar code on the cartridge and identifies the type of cartridge for operator confirmation. Blood (collected in a 3.2% sodium citrate tube) or Quality Control (QC) material is added to the entry port on the cartridge and drawn into the cartridge under the TEG® 6s Hemostasis analyzer control. The amount of the sample drawn into the cartridge is determined by the pre-set volume of the blood chambers in the cartridge. Once in the cartridge, the sample is metered into as many as 4 separate analysis channels, depending upon the assays being performed. Reconstitution of reagents dried within the cartridge is accomplished by moving the sample back and forth through reagent chambers, under the control of microfluidic valves and bellows (pumps) within the cartridge. After each sample has been mixed with reagent, it is delivered to a test cell where it is monitored for viscoelastic changes due to coagulation. Excess sample material is moved under microfluidic control into an enclosed waste chamber within the cartridge.

The TEG® 6s Measurement Technique

The TEG® 6s technology is based on a 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 test tube (ring) and the resonant frequency will rise with increasing firmness of the clot. The TEG® 6s Hemostasis Analyzer collects meniscus motion data, tracks changing resonant frequencies and analyzes the frequency data to provide semi-quantitative parameters describing the clot. Results are presented in a format similar to the TEG® 5000.

Both the TEG® 5000 and TEG® 6s Hemostasis System monitors the interaction of platelets within the fibrin mesh of the clot during clot formation and lysis, all in a whole-blood setting. Like the TEG® 5000, the TEG® 6s Hemostasis System uses thromboelastography to provide continuous measurement of clot elasticity. Method Comparison testing has been performed, yielding data from12 clinical sites. These data include the applicable parameters for the tests in the TEG® 6s Citrated: K, RT, FF Assay Cartridge. The TEG® 5000 System measures the changes of the linkage forces of the clot between the cup and pin over time, while the TEG® 6s Hemostasis System measures the changes of the resonant frequency of the clot over time. Despite the difference in the way the 2 analyzers measure the changes in the modulus of elasticity of the clot over time, they measure the same physical phenomenon and produce the same result when converted from their specific units of measurement (forces for the TEG® 5000 System and frequency for the TEG® 6s Hemostasis System) to millimeters. The fact that these results are similar across all reagents used in both technologies is demonstration that the 2 technologies measure the same phenomenon, the changes in elastic modulus. Table 1 provides the following definitions that apply to calculated parameters in the TEG® 6s Hemostasis System.

Table 1. TEG® 6s parameter definitions

TEG® 6s Parameter	Definition	Parameter Relation to Hemostasis
R	R is the time from the start of the test until initial fibrin formation. This represents the enzymatic portion of coagulation.	Normal / reduced / increased speed of coagulation initiation
MA	MA, or Maximum Amplitude, represents the maximum firmness of the clot during the test.	Normal / reduced / increased clot elasticity/strength
LY30	LY30 is a measurement of the rate of fibrinolysis 30 minutes after MA is reached. The LY30 measurement is based on the reduction of the tracing area that occurs between the time that MA is measured until 30 minutes after the MA is defined.	Normal / reduced clot stability; clot dissolution

HAEMONETICS®

Citrated Assays

CK assay

The CK assay is a semi-quantitative in vitro diagnostic assay for monitoring the hemostasis process via the intrinsic pathway in citrated whole blood specimens on the TEG® 6s Hemostasis System. The CK assay consists of Kaolin. Kaolin is used in the assay for activation of coagulation. It is combined with calcium chloride to neutralize the sodium citrate used to anticoagulate the blood sample. The CK hemostasis profile resulting from kaolin activation provides a measure of the time it takes for the first measurable clot to be formed, the kinetics of clot formation, the strength of the clot and the breakdown of the clot, or fibrinolysis.

The clotting characteristics of the CK generated hemostasis profile are described by the functional parameters Clotting Time (R) and Clot Lysis measured thirty minutes after MA (LY30). Since it may take an hour or more for a non-activated whole blood sample to reach maximum amplitude MA, Kaolin is essential to reduce run time and variability associated with running non-activated whole blood samples.

CRT assay

The CRT assay is a semi-quantitative in vitro diagnostic assay for monitoring the hemostasis process via both the intrinsic and extrinsic pathway in citrated whole blood specimens on the TEG® 6s Hemostasis System. The CRT is an accelerated assay consisting of Kaolin and Tissue Factor. As described in the CK assay, Kaolin is used for activation of coagulation and is combined with Calcium Chloride to neutralize sodium citrate in the blood sample. The addition of Tissue Factor is used for coagulation activation that would be classically described as extrinsic. The CRT hemostasis profile resulting from Kaolin and Tissue Factor activation provides a measure of the strength of the clot and the breakdown of the clot, or fibrinolysis.

The clotting characteristics of the CRT generated hemostasis profile are described by the functional parameter Maximum Clot Strength (MA). The CRT assay produces an accelerated clotting time which allows for an earlier MA result compared to the CK assay. Therefore, in the TEG® Hemostasis System, the CRT assay is simultaneously run along with the CK assay to provide a fast way to reach a stable value for MA (CRT) while still measuring the time-dependent parameters (CK).

CFF assay

The CFF assay is a semi-quantitative in vitro diagnostic assay for monitoring the hemostasis process after blocking platelet contributions to clot strength in citrated whole blood specimens on the TEG® 6s Hemostasis System. The CFF assay consists of Tissue Factor and abciximab (ReoPro®). It is combined with Calcium Chloride to neutralize sodium citrate in the blood sample. Tissue Factor is used for coagulation activation that would be classically described as extrinsic,

with platelet aggregation inhibited by abciximab (a GPIIb/IIIa inhibitor), excluding its contribution to clot strength, and thereby measuring fibrinogen contribution to clot strength.

The clotting characteristics of the CFF generated hemostasis profile are described by the functional parameter Maximum Clot Strength (MA) and measures the part of clot strength that is contributed by fibrinogen in the blood sample.

INTENDED USE/INDICATIONS FOR USE:

TEG® 6s Hemostasis System for use with the TEG® 6s Citrated: K, RT, FF Assay Cartridge
Intended Use/Indications for Use

The TEG 6s Hemostasis System consists of the TEG 6s Hemostasis Analyzer and TEG 6s Citrated: K, RT, FF Assay Cartridge. The TEG 6s Hemostasis System is intended for in vitro diagnostic use to provide semi-quantitative indications of the hemostasis state of a venous blood sample. The TEG 6s Hemostasis System records the kinetic changes in a sample of 3.2% citrated whole blood as the sample clots.

The Citrated: K, RT, FF Assay Cartridge contains three independent assays (CK, CRT and CFF) and the system output consists of a table of numerical values for parameters R, LY30, and MA.

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 LY30 (fibrinolysis after 30 minutes of reaching maximum clot strength).

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 Hemostasis System. Clotting characteristics are described by the functional parameter MA (maximum clot strength).

The CFF assay monitors hemostasis of 3.2% citrated whole blood specimens in the TEG 6s Hemostasis System after blocking platelet contributions to clot strength. Clotting characteristics are described by the functional parameter MA (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. The indication for TEG 6s Hemostasis System use is with adult patients (18 years and older) where an evaluation of their blood hemostasis properties is desired. Hemostasis evaluation with the TEG 6s Hemostasis System using the Citrated: K, RT, FF Assay Cartridge is used to assess clinical conditions in a trauma setting to assess hemorrhage or thrombosis conditions.
For professional use only.

HAEMONETICS®

SUMMARY OF TECHNOLOGICAL CHARACTERISTICS COMPARING THE TEG® 6s HEMOSTATSIS SYSTEM TO THE TEG® 5000 PREDICATE DEVICE

Tables 2 and 3 provide a summary of the similarities and differences of the TEG® 6s Hemostasis system and the TEG® 5000 predicate device, respectively.

Table 2. Table of Similarities

Item	TEG® 5000 System Predicate	TEG® 6s Hemostasis System
Analyzer		
Technological Purpose	Monitoring the response of a clot to low levels of applied strain (resonance frequency)	Monitoring the response of a clot to low levels of applied strain (resonance frequency)
Measurement	Changes in physical clot elasticity over time	Changes in physical clot elasticity over time
Initial Warm Up Time	5 min	5 min
Time to Complete a Test	Varies with assay	Varies with assay
Measurement Output	Graphical tracings of resonant frequency per reagent type; table of parameters	Graphical tracings of resonant frequency per reagent type; table of parameters
Assay and Reagents		
Citrated Kaolin (CK)	Kaolin and CaCl2	Kaolin and CaCl2, same materials as TEG® 5000
Citrated RapidTEG™ (CRT)	Tissue Factor (TF), Kaolin and CaCl2	Tissue Factor (TF), Kaolin and CaCl2 , same materials as TEG® 5000
Citrated Functional Fibrinogen (CFF)	Abciximab, Tissue Factor and CaCl2	Abciximab, Tissue Factor and CaCl2, same materials as TEG® 5000

Table 3. Table of Differences

Item	TEG® 5000 System Predicate	TEG® 6s Hemostasis System
Analyzer	Thrombelastography analyzer, separate computer and software	Fully integrated Thrombelastography analyzer
Measuring Technique	Direct-contact measurement of shear elasticity of a coagulating sample	Non-contact measurement of shear elasticity of a coagulating sample

HAEMONETICS®

Item	TEG® 5000 System Predicate	TEG® 6s Hemostasis System
Measuring Channels	Two, each independent and interchangeable (can be used with any approved reagent)	Four, each independent and interchangeable (can be used with any approved reagent)
Signal Transducer	Electromechanical detection (rotary variable inductive transformer) of rotary motion of a pin suspended in the sample	Optical detection (silicon photodiode) of the motion of a free surface of the sample
Temperature Control	20° to 40°C	20° to 50°C
Sample Volume (per channel)	360-380 µl	20 µl
Total Reaction Volume (single channel)	360-380 µl	20 µl
Mains Supply Voltage	120V, 60Hz and 220V, 50Hz model available	100-240V, 50-60Hz (international power supply)
Analyzer Input Voltage	24 volts AC, 30 watts max	12 volts DC, 60 watts max
Environment	Level and vibration free position, no solar radiation Operating temperature: 10° to 35 °C Storage Temperature: -30° to +50 °C (analyzer only) Relative humidity 20-80% (non-condensing)	Stable and level surface Operating Temperature 10° to 32°C Storage Temperature: -20° to 50°C (analyzer only) Relative humidity 20 to 80% (non-condensing)
Sample Preparation	Performed by the operator using pipettes to reconstitute reagents and mix reagents with the sample	Performed under analyzer control within the disposable cartridge
Pipetting	Manual accurate pipettes (10, 20, 50, 100, 340, 360, 500, 1000µl)	Unmetered transfer pipette or syringe; blood sample is added until it fills to a level above the line marked on the blood intake well of the cartridge
Analyzer Software	Thrombelastography analyzer, separate computer and software	Fully integrated Thrombelastography analyzer

Item	TEG® 5000 System Predicate	TEG® 6s Hemostasis System
Consumables	Cups & Pins (acrylic plastic)	Carrier (acrylic plastic) with microfluidics laminate and test rings (acrylic plastic)

SUMMARY OF PERFORMANCE DATA

Electrical safety and electromagnetic compatibility (EMC)

Electrical safety and EMC testing were conducted on the TEG® 6s Hemostasis analyzer. The system complies with the IEC 60601-1, IEC 60601-2-10, IEC 60601-2-81, IEC 60601-2-101 and UL 61010-1 standards for safety and the IEC 60601-1-2, EN61326-1, EN61326-2-6, EN61000-3-2, EN61000-3-3 and EN55011 standards for EMC.

Software Verification and Validation Testing

Software verification and validation testing were conducted and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered as a "moderate" level of concern since there is no direct patient contact, any possible injury to a patient is indirect.

Performance Testing

Reference Ranges

Reference Ranges were established according to CLSI C28-A3c. Citrated whole blood from normal donors (representative of normal population distributions –age, gender, race) with no known coagulopathies and not taking any drugs that would potentially affect patient hemostasis was used. Non-parametric method for analysis was used to determine the reference range for each assay parameter. Table 4 contains the reference range data for each assay parameter.

Table 4. Reference Ranges Summary

Reagent/Parameter	Min	Max	Sample size
CK R (minutes)	4.6	9.1	157
CK LY30 (percent)	0.0	2.6	132
CRT MA (mm)	52	70	152
CFF MA (mm)	15	32	151

Analytical Precision

Testing was performed for precision, using CLSI EP5-A2 as guidance. Three types of donor citrated whole blood were used in this precision testing:

- Hypo: donors with natural coagulation levels of R parameter near the upper limit of the reference range and MA parameter near the lower limit of the reference range;

- Normal: donors with natural coagulation levels of R and MA parameters near the center of the reference ranges;
- Hyper: donors with natural coagulation levels of R parameter near the lower limit of the reference range and MA parameter near the upper limit of the reference range

Testing was performed with blood from 4 donors (2 Hypo, 1 Normal and 1 Hyper) run in duplicate, 2 operators using 3 reagent lots and 12 analyzers for 5 non-consecutive days

Precision test estimates by test, parameter and donor sample test level are shown in Table 5.

HAEMONETICS®

Table 5. Precision Summary

Test	Parameter	Level	n	Mean	Reagent Lot		Operator		Instrument*		Day**		Repeatability		Total^	
					SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
CK	R	Hypo1	120	8.9	0	0.0	0.29	3.3	0	0.0	0.64	7.1	0.85	9.5	0.9	10.0
CK	R	Hypo2	120	6.6	0	0.0	0	0.0	0	0.0	0.76	12.0	0.77	12.0	0.77	12.0
CK	R	Norm	120	6.5	0	0.0	0	0.0	0	0.0	0.28	4.3	0.49	7.6	0.49	7.6
CK	R	Hyper	120	5.2	0.13	2.5	0	0.0	0	0.0	0.31	5.8	0.66	13.0	0.67	13.0
CRT	MA	Hypo1	120	63.8	0	0.0	0.09	0.1	0.09	0.1	0.28	0.4	0.33	0.5	0.35	0.6
CRT	MA	Hypo2	120	52.4	0.39	0.7	0.22	0.4	0	0.0	0.92	1.8	0.59	1.1	0.74	1.4
CRT	MA	Norm	120	62.7	0	0.0	0.15	0.2	0.14	0.2	0.37	0.6	0.31	0.5	0.37	0.6
CRT	MA	Hyper	120	69.4	0	0.0	0	0.0	0	0.0	0.91	1.3	0.2	0.3	0.2	0.3
CFF	MA	Hypo1	120	21.0	0	0.0	0.15	0.7	0.08	0.4	0.33	1.6	0.31	1.5	0.36	1.7
CFF	MA	Hypo2	120	14.8	0.11	0.8	0	0.0	0	0.0	0.29	2.0	0.33	2.2	0.35	2.3
CFF	MA	Norm	120	20.6	0	0.0	0.13	0.6	0	0.0	0.3	1.5	0.22	1.1	0.25	1.2
CFF	MA	Hyper	120	32.7	0	0.0	0	0.0	0	0.0	2.71	8.3	0.53	1.6	0.53	1.6

* within Operator, Reagent Lot; ** within instrument, operator, reagent lot, ^ within day

A second precision study was performed to supplement the above precision data. Three types of citrated whole blood samples were used in this precision testing:

- Hypo (contrived): blood from normal donors with natural coagulation levels of R and MA parameters near the center of the reference ranges, spiked with high concentrations of Dabigatran to increase the R parameter and Cytochalasin D and ReoPro® to reduce the MA parameter.
- Hyper (contrived): blood from normal donors with natural coagulation levels of R and MA parameters near the center of the reference ranges, spiked with Kaolin solution to reduce the R parameter and RiaStap® (fibrinogen) to increase the MA parameter.
- Hypo (patient-derived): blood from clinical patients being treated with therapeutic levels of anticoagulants (Dabigatran or Warfarin (Coumadin))

Testing was performed with 3 contrived samples for the Hypo (contrived) and Hyper (contrived) types, 4 patient-derived dabigatran samples and 2 patient-derived warfarin samples run in duplicate, 3 operators using 3 reagent lots and up to 12 analyzers.

Precision test estimates by test, parameter and donor sample test level are shown in Tables 6 and 7.

HAEMONETICS®

Table 6. Precision summary for contrived samples

Test	Parameter	Contrived Sample type	Patient ID	N	Mean	Lot		Operator		Instrument		Repetition		Total	
						SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
CK	R	hyper	D101	12	2.1	0.0	0.0	0.0	0.0	0.1	4.5	0.1	3.1	0.1	5.5
CK	R	hyper	D108	12	2.7	0.0	0.0	0.0	1.0	0.1	3.5	0.1	2.4	0.1	4.3
CK	R	hyper	D169	12	2.2	0.1	2.8	0.0	0.0	0.1	3.0	0.1	2.5	0.1	4.6
CK	R	hypo	D141	12	16.1	0.0	0.0	1.1	6.9	1.3	8.0	0.7	4.3	1.7	10.8
CK	R	hypo	D169	12	15.3	0.8	5.3	0.0	0.0	1.6	10.2	1.1	7.1	2.0	13.2
CK	R	hypo	D108	12	12.1	0.1	1.0	0.1	0.9	0.9	7.2	0.7	5.6	1.1	9.3
CRT	MA	hyper	D108	12	70.8	0.2	0.3	0.0	0.0	0.1	0.2	0.1	0.2	0.2	0.3
CRT	MA	hyper	D121	12	72.5	0.2	0.3	0.0	0.0	0.4	0.5	0.4	0.5	0.5	0.8
CRT	MA	hyper	D145	12	73.0	0.2	0.2	0.0	0.0	0.2	0.3	0.2	0.2	0.3	0.4
CRT	MA	hypo	D141	12	41.3	0.0	0.0	0.0	0.0	0.7	1.8	0.5	1.2	0.9	2.2
CRT	MA	hypo	D169	12	44.4	0.0	0.0	0.3	0.7	0.6	1.3	0.4	0.9	0.8	1.7
CRT	MA	hypo	D108	12	45.5	0.0	0.0	0.4	0.9	1.0	2.1	0.5	1.1	1.1	2.5
CFF	MA	hyper	D101	12	49.9	0.1	0.1	0.0	0.0	0.5	0.9	0.3	0.5	0.5	1.1
CFF	MA	hyper	D141	12	44.3	0.0	0.0	0.0	0.0	0.5	1.2	0.3	0.6	0.6	1.3
CFF	MA	hyper	D145	12	47.0	0.0	0.0	0.0	0.0	0.7	1.4	0.5	1.0	0.8	1.7
CFF	MA	hypo	D101	12	10.2	0.2	1.5	0.0	0.0	0.3	3.0	0.2	1.7	0.4	3.6
CFF	MA	hypo	D125	12	9.5	0.0	0.0	0.2	1.8	0.4	4.0	0.3	2.7	0.5	5.0
CFF	MA	hypo	D169	12	6.5	0.0	0.0	0.7	10.1	0.3	4.9	0.4	6.0	0.8	11.6

Table 7. Precision summary for patient-derived samples

Test	Parameter	Patient ID	N	Mean	Lot		Operator		Instrument		Repetition		Total	
					SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
CK	R	MH-DB001	12	13	0.0	0.0	0.0	0.0	0.4	3.2	1.2	8.9	1.2	9.4
CK	R	MH-DB002	12	21.3	0.0	0.0	0.0	0.0	1.0	4.7	2.1	10.1	2.3	11.0
CK	R	MH-DB003	12	14.4	0.0	0.0	0.0	0.0	0.0	0.0	2.4	16.9	2.4	16.9
CK	R	MH-DB004	12	11.8	0.5	4.0	0.5	4.3	0.0	0.0	1.6	13.9	1.7	14.8
CK	R	MH-WR001	12	9.9	0.7	7.0	0.3	2.7	0.3	2.6	0.5	4.9	0.8	8.5
CK	R	MH-WR002	12	10.1	1.0	10.2	0.0	0.0	0.3	3.2	1.0	10.0	1.4	13.6
CRT	MA	MH-DB001	12	64.9	0.1	0.1	0.0	0.0	0.1	0.1	0.1	0.2	0.1	0.2
CRT	MA	MH-DB002	12	67.7	0.1	0.1	0.0	0.0	0.0	0.0	0.2	0.2	0.2	0.2
CRT	MA	MH-DB003	12	66.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.2	0.1	0.2
CRT	MA	MH-DB004	12	73.8	0.1	0.1	0.0	0.0	0.1	0.1	0.2	0.2	0.2	0.3
CRT	MA	MH-WR001	12	64.0	0.1	0.1	0.0	0.0	0.0	0.0	0.2	0.3	0.2	0.3
CRT	MA	MH-WR002	12	64.7	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.4	0.3	0.4
CFF	MA	MH-DB001	12	20.7	0.1	0.4	0.0	0.0	0.3	1.3	0.1	0.6	0.3	1.4
CFF	MA	MH-DB002	12	23.7	0.3	1.3	0.3	1.4	0.0	0.0	0.2	0.7	0.4	1.6
CFF	MA	MH-DB003	12	23.4	0.2	1.0	0.0	0.0	0.0	0.0	0.3	1.5	0.4	1.7
CFF	MA	MH-DB004	12	51.9	1.1	2.2	0.0	0.0	0.0	0.0	0.4	0.8	1.1	2.0
CFF	MA	MH-WR001	12	20.7	0.0	0.0	0.0	0.0	0.0	0.0	0.4	1.7	0.4	1.7
CFF	MA	MH-WR002	12	24.7	0.1	0.4	0.3	1.2	0.0	0.0	0.3	1.3	0.4	1.7

DB – Dabigatran; WR – Warfarin

A third precision study was performed to support the precision of the CK LY30 parameter. Testing was performed for precision, using CLSI EP5-A2 as guidance. Three types of citrated whole blood samples were used in this precision testing:

- no tPA: blood from normal donors
- low tPA (contrived): blood from a normal donor spiked to create a low tPA blood sample
- high tPA (contrived): blood from a normal donor spiked to create a high tPA blood sample

Testing was performed with the 3 sample types (no tPA, low tPA, high tPA) 12 replicates/sample type using 3 operators using 3 reagent lots for 5 days. Precision test estimates by test, parameter and sample test level are shown in Table 8.

HAEMONETICS®

Table 8. CK LY30 Precision Summary

Donor	Sample	N	Mean	Within Day		Between Operator		Between Cartridge		Between Day		Total		Total (Descriptive	
				SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
146	High Lysis	60	26.23	1.22	5	0.00	0	0.74	3	1.35	5	1.96	7	1.86	7
	Low Lysis	60	7.44	1.08	14	0.00	0	0.28	4	0.84	11	1.40	19	1.29	17
	No Lysis	60	1.01	0.30	30	0.09	8	0.00	0	0.22	21	0.38	38	0.35	35
147	High Lysis	60	25.15	1.19	5	0.00	0	1.14	5	3.21	13	3.61	14	3.22	13
	Low Lysis	60	5.09	0.00	0	0.23	5	0.00	0	0.91	18	1.27	25	1.08	21
	No Lysis	60	0.46	0.23	49	0.12	26	0.00	0	0.15	33	0.30	65	0.28	63
100287	High Lysis	59	17.82	1.10	6	0.59	3	0.49	3	1.12	6	1.68	9	1.68	9
	Low Lysis	58	5.03	0.63	13	0.00	0	0.54	11	0.96	19	1.27	25	1.14	23
	No Lysis	58	1.2	0.28	23	0.07	6	0.00	0	0.17	14	0.32	27	0.32	27

Interference

Testing was performed for interference following CLSI EP7-A2 as guidance.

For the CK assay, potential interfering factors tested were Absence of a Discard Tube, Short Draw, Hemolysis, Hemodilution, Direct Oral Anticoagulants (FXa and direct thrombin inhibitors), and Antiplatelet Drug (P2Y12 inhibitor). None were found to be interfering factors.

For the CRT assay, potential interfering factors tested were Absence of a Discard Tube, Short Draw, Hemolysis, Hemodilution, Direct Oral Anticoagulants (FXa and direct thrombin inhibitors), and Antiplatelet Drug (P2Y12 inhibitor). Only Hemolysis and Hemodilution above 30% were found to be interfering factors.

For the CFF assay, potential interfering factors tested were Absence of a Discard Tube, Short Draw, Hemolysis, Hemodilution, Direct Oral Anticoagulants (FXa and direct thrombin inhibitors), and Antiplatelet Drug (P2Y12 inhibitor). Only Hemodilution above 40% was found to be an interfering factor.

Measurement Interpretation Guidance

The measurement interpretation table below is based on in vitro studies that examined individual values of assays and parameters with respect to their reference ranges. Only one or a few variables influencing TEG results were systematically varied while other variables were kept constant.

The measurement interpretation guidance table is not intended to be comprehensive of all variables that could influence test results, but addresses key variables based on literature review and clinical experience. As with any hemostasis test, TEG 6s test results 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. Refer to Table 9.

Table 9. TEG® 6s Measurement Interpretation Guidance

Assay	Parameter (Units)	Ref Range (RR)	Parameter Readout	Hemostatic Significance of Individual Parameter	Interpretation of Parameter Readout for Consideration	References
CK	R (min)	4.6-9.1	CK R > RR	Hypocoagulable	↓ Coagulation factor activity and/or presence of heparin at sufficiently high concentrations+	1-4, 17, 26
			CK R < RR	Hypercoagulable		24, 28
	LY30 (%)	0-2.6	CK LY30 > RR	Hypocoagulable	Hyperfibrinolysis	5-11, 16, 19-20, 23
CRT	MA (mm)	52-70	CRT MA < RR	Hypocoagulable	↓ Fibrinogen or ↓ platelet contribution ++	8, 10, 12, 13, 18, 21, 25, 27
			CRT MA > RR	Hypercoagulable	↑ Platelet contribution++	
CFF	MA (mm)	15-32	CFF MA < RR	Hypocoagulable	↓ Fibrinogen++	7, 10, 12, 14-15, 22, 25, 27
			CFF MA > RR	Hypercoagulable	↑ Fibrinogen++	

Note: These findings were supported by in vitro studies.

+ Detection thresholds were 0.1 IU/mL for unfractionated heparin and 0.3 IU/mL for low molecular weight heparin, respectively in *in vitro* experiments. Actual threshold values in patients may differ. Heparinization can be exogenous or endogenous [26]

++ Other factors, such as factors of the coagulation cascade and FXIII, may contribute to clot stiffness.

Citrated Kaolin (CK)

The standard Citrated Kaolin TEG® assay uses kaolin for activation of coagulation. Kaolin activation has traditionally been described as intrinsic pathway activation. The hemostasis profile resulting from kaolin activation provides a measure of the time it takes for the first measurable clot to be formed, the kinetics of clot formation, the strength of the clot and the breakdown of the clot, or fibrinolysis.

CK R

Kaolin R is the time in minutes elapsing between sample activation and the point in time where clotting provides enough resistance to produce a 2 mm amplitude reading on the TEG® analyzer tracing. The CK R parameter represents the initiation phase of coagulation triggered by enzymatic clotting factors and culminating with the initial fibrin formation. A prolonged R value is indicative of slow clot formation, and a shortened R value indicative of fast clot formation.

Clinical Value. A prolonged R value is indicative of slow clot formation, due to coagulation factor deficiencies or heparin.[1-4, 17,26] A shortened CK R time has been observed in patients post traumatic injury.[28]

CK LY30

Kaolin LY30 is the percent lysis based on the reduction of the tracing area that occurs between the time maximal amplitude (MA) is measured until 30 minutes after the MA is defined. After the clot has formed, it is degraded by fibrinolytic factors within the blood and consequently the amplitude decreases over time. By measuring the extent of amplitude reduction over time, clot lysis can be assessed.

Clinical Value. LY30 provides information about patient fibrinolysis and potential pathologies.[5-11,16,19,20,23]

Citrated RapidTEG™ (CRT)

The RapidTEG assay incorporates both tissue factor and kaolin, which simultaneously activates the intrinsic and extrinsic coagulation pathways. The assay accelerates coagulation compared to the conventional Kaolin test.

CRT MA

RapidTEG™ MA is the point of maximal amplitude of the TEG® tracing, measured in mm, and reflects the maximum clot strength. The strength of the clot is primarily a result of platelet–fibrin interactions via the GPIIb/IIIa receptors.[15]

Clinical Value. The MA provides information, in combination with CFF MA, of the contribution of platelets to the overall strength of the clot. A decreased MA is indicative of low clot strength, which could be due to decreased platelet contribution or decreased fibrinogen, whereas an increased MA is indicative of high clot strength, which could be due to increased platelet contribution.[8,10,12,13,18,21,25,27]

Citrated Functional Fibrinogen (CFF)

The Citrated Functional Fibrinogen assay activates the extrinsic pathway using tissue factor and inhibits platelet aggregation using a platelet inhibitor that binds to GPIIb/IIIa receptors.

CFF MA

The Functional Fibrinogen reagent inhibits platelet aggregation via the GPIIb/IIIa receptor, excluding its contribution to clot strength (MA) and thereby primarily measures the fibrinogen contribution to clot strength.

Clinical Value: CFF MA provides the overall contribution of fibrinogen and/or platelet contribution to clot strength. In conjunction with CRT, this assay enables the contributions of fibrin and platelets to clot strength to be determined.[7,10,12,14,15,22,25,27]

Method Comparison

A method comparison study was conducted at 12 US clinical sites collecting patient samples following CLSI EP09-A3 Guidelines. Enrolled were adult patients (male or females 18 years of age and older) who met the full or limited trauma team criteria of the American College of Surgeons or similar criteria established per institutional guidelines.

The assessment of equivalency between the two devices was primarily based on the assessment of predicted bias at the reference range limits relative to the predefined acceptable limits of the bias. Further assessment of equivalency was based on evaluating the estimate of the slope of the linear regression line. An additional evaluation was based on the assessment of the predicted bias at the limits of the analytical measurement range (AMR) and the estimate of the Pearson linear correlation.

The linear regression slope estimates for all between device comparisons were close to 1.0 with their respective 95% confidence intervals all containing 1.0. The slope estimates for all parameters ranged from 0.99 to 1.06.

For all parameters, the assessment of predictive bias and its 95% confidence interval relative to the bias acceptance criteria supports equivalency according to the CLSI EP09-A3. Predicted biases at the AMR limits were consistent with bias predictions at the reference range limits.

Pearson linear correlation estimates were above 0.9 for all identical parameters. In addition, the between device correlation of CRT MA (TEG® 6s) and CK MA (TEG® 5000) was 0.86.

In summary, the method comparison data strongly supports the correlation between TEG® 6s and the TEG® 5000 in patients with known or suspected traumatic injury. Refer to Table 10.

Table 10. Method Comparison Summary Table for TEG® 6s and TEG® 5000

Assay Parameter	N	Spike	Slope	Correlation	AMR Point 1	AMR Bias 1	AMR Point 2	AMR Bias 2	Ref Point 1	Ref Bias 1	Ref Point 2	Ref Bias 2
CFF MA	450	30	0.99 [0.94, 1.03]	0.95 [0.94, 0.96]	4	-2.01 [-2.77, -1.23]	52	-2.6 [-4.29, -1.08]	15	-2.14 [-2.44, -1.87]	32	-2.35 [-3.04, -1.75]
CK R	405	36	1.05 [1, 1.1]	0.9 [0.88, 0.91]	0.4	0.55 [0.31, 0.79]	17	1.33 [0.7, 1.95]	4.6	0.75 [0.64, 0.85]	9.1	0.96 [0.72, 1.2]
CK LY30	86	17	1.01 [0.91, 1.1]	0.91 [0.87, 0.94]	0	0.48 [-0.12, 1.08]	22	0.6 [-1.22, 2.41]	0	0.48 [-0.12, 1.08]	2.6	0.49 [0, 0.98]
CRT MA vs. CK MA*	336	0	1.06 [0.99, 1.12]	0.86 [0.83, 0.89]	40	-5.31 [-6.95, -3.66]	75	-3.31 [-4.12, -2.51]	52	-4.62 [-5.51, -3.73]	70	-3.6 [-4.13, -3.06]

AMR – Analytical Measurement Range; Ref – Reference Range; Point 1/Bias 1 – Lower Limit; Point 2/Bias 2 – Upper Limit

* The TEG® 6s CRT MA parameter was compared to the TEG® 5000 CK MA parameter to demonstrate that the CRT MA parameter is equivalent to the CK MA Parameter but the final MA value is reached more quickly using the CRT assay.

CONCLUSIONS DRAWN FROM PERFORMANCE TESTING

The performance data and information provided in this submission support a substantial equivalence determination for the TEG® 6s Hemostasis System and the TEG® 5000 predicate device.

REFERENCES

1. Da Luz LT, Nascimento B, Shankarakutty AK, Rizoli S, Adhikari NK. Effect of thromboelastography (TEG®) and rotational thromboelastometry (ROTEM®) on diagnosis of coagulopathy, transfusion guidance and mortality in trauma: descriptive systematic review. Crit Care. 2014;18(5):518.
2. Kang Y. Thromboelastography in liver transplantation. Semin Thromb Hemost. 1995;21(S04): 034-044.
3. Nielsen VG, Cohen BM, Cohen E. Effects of coagulation factor deficiency on plasma coagulation kinetics determined via thrombelastography®: critical roles of fibrinogen and factors II, VII, X and XII. Acta Anaesthesiologica Scandinavica. 2005;49:222-231.
4. Zmuda K, Neofotistos D, Ts'ao C. Effects of unfractionated heparin, low-molecular-weight heparin, and heparinoid on thromboelastographic assay of blood coagulation. American Journal of Clinical Pathology. 2000;113(5):725-731.
5. ACS TQIP massive transfusion in trauma guidelines. https://www.facs.org/~/media/files/quality programs/trauma/tqip/massive transfusion in trauma guildelines.ashx. Accessed February 6, 2019.
6. Cotton BA, Minei KM, et al. Admission rapid thrombelastography predicts development of pulmonary embolism in trauma patients. Journal of Trauma and Acute Care Surgery. 2012;72(6):1470–1477.
7. Gonzalez E, Moore EE, Moore HB, et al. Trauma-induced coagulopathy: an institution's 35 year perspective on practice and research. Scand J Surg. 2014;103(2):89-103.
8. Gonzalez E, Moore EE, Moore HB. Management of trauma-induced coagulopathy with thrombelastography. Crit Care Clin. 2017;33(1):119-134.
9. Gonzalez E, Moore EE, Moore HB, et al. Goal-directed hemostatic resuscitation of trauma-induced coagulopathy: a pragmatic randomized clinical trial comparing a viscoelastic assay to conventional coagulation assays. Ann Surg. 2016;263(6):1051-9.
10. Johansson PI, Sørensen AM, Larsen CF, et al. Low hemorrhage-related mortality in trauma patients in a Level i trauma center employing transfusion packages and early thromboelastography-directed hemostatic resuscitation with plasma and platelets. Transfusion. 2013;53(12):3088-3099.
11. Chapman MP, Moore EE, Moore HB, et al. Overwhelming tPA release, not PAI-1 degradation, is responsible for hyperfibrinolysis in severely injured trauma patients. J Trauma Acute Care Surg. 2016;80(1):16-23.

12. Kornblith LZL, Kutcher MEM, Redick BJ, Calfee CS, Vilardi RF, Cohen MJ. Fibrinogen and platelet contributions to clot formation: Implications for trauma resuscitation and thromboprophylaxis. J Trauma Acute Care Surg. 2014;76(2):255-6-3.
13. Oshita K, Az-Ma T, Osawa Y, Yuge O. Quantitative measurement of thromboelastography as a function of platelet count. 1999.
14. Harr JN, Moore EE, Ghasabyan A, et al. Functional fibrinogen assay indicates that fibrinogen is critical in correcting abnormal clot strength following trauma. Shock. 2013;39(1):45-49.
15. Kawasaki J, Katori N, Kodaka M, Miyao H. Electron microscopic evaluations of clot morphology during thrombelastography. Anesth Analg. 2004;99(5):1440-4.
16. Chapman MP, Moore EE, Ramos CR, et al. Fibrinolysis greater than 3% is the critical value for initiation of antifibrinolytic therapy. J Trauma Acute Care Surg. 2013;75(6):961-7.
17. Nascimento B, Al Mahoos M, Callum J, et al. Vitamin K-dependent coagulation factor deficiency in trauma: a comparative analysis between international normalized ratio and thromboelastography. Transfusion. 2012;52(1):7-13.
18. Bowbrick VA, Mikhailidis DP, Stansby G. Influence of platelet count and activity on thromboelastography parameters. Platelets. 2003;14(4):219-224.
19. Cotton B a, Harvin J a, Kostousouv V, et al. Hyperfibrinolysis at admission is an uncommon but highly lethal event associated with shock and prehospital fluid administration. J Trauma Acute Care Surg. 2012;73(2):365-70.
20. Harvin JA, Peirce CA, Mims MM, et al. The impact of tranexamic acid on mortality in injured patients with hyperfibrinolysis. J Trauma Acute Care Surg. 2015;78(5):905-9.
21. Liu C, Guan Z, Xu Q, et al. Relation of thromboelastography parameters to conventional coagulation tests used to evaluate the hypercoagulable state of aged fracture patients. Medicine (Baltimore). 2016;95(24):e3934.
22. Meyer M a S, Ostrowski SR, Sørensen AM, et al. Fibrinogen in trauma, an evaluation of thrombelastography and rotational thromboelastometry fibrinogen assays. J Surg Res. 2014:1-10.
23. Khan M, Jehan F, Bulger EM, et al. Severely injured trauma patients with admission hyperfibrinolysis: Is there a role of tranexamic acid? Findings from the PROPPR trial. J Trauma Acute Care Surg. 2018;85(5):851-857.
24. Toukh M, Siemens DR, Black A, et al. Thromboelastography identifies hypercoagulablilty and predicts thromboembolic complications in patients with prostate cancer. Thromb Res. 2014;133(1):88-95.
25. Erdoes G, Schloer H, Eberle B, et al. Next generation viscoelasticity assays in cardiothoracic surgery: Feasibility of the TEG6s system. PLoS One. 2018;13(12).
26. Ostrowski SR, Johansson PI. Endothelial glycocalyx degradation induces endogenous heparinization in patients with severe injury and early traumatic coagulopathy. J Trauma Acute Care Surg. 2012;73(1):60-66.

27. Noorman F, Hess JR. The contribution of the individual blood elements to the variability of thromboelastographic measures. Transfusion. 2018;58(10):2430-2436.
28. Schreiber MA, Differding J, Thorborg P, et al. Hypercoagulability is most prevalent early after injury and in female patients. J Trauma. 2005;58(3):475-80.