510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:
k101533

B. Purpose for Submission:
Bundled submission for clearance of new assays

C. Measurand:
Coagulation Factors (extrinsic pathway)

D. Type of Test:
Clotting

E. Applicant:
TEM Innovations GmbH

F. Proprietary and Established Names:
EXTEM® Assay, FIBTEM® Assay, APTEM® Assay for the ROTEM® *delta* Thromboelastometry System
ROTROL N
ROTROL P

G. Regulatory Information:

1. Regulation section:
   21 CFR §864.5425 - Multipurpose system for *in vitro* coagulation studies
2. Classification:
   Class II
3. Product code:
   JPA – System, Multipurpose for *in vitro* coagulation studies
4. Panel:
   81 Hematology

H. Intended Use:

1. Intended use(s):
   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* 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).

2. Indication(s) for use:
   Each assay, APTEM, EXTEM and FIBTEM is performed on the ROTEM delta analyzer which has the following indication for use:

   The indication for ROTEM® *delta* is in adult patients when an evaluation of their blood coagulation properties is desired. Coagulation evaluations with the ROTEM® *delta* system are commonly used to assess clinical conditions in organ transplantation, cardiovascular surgery, cardiology procedures and trauma to access post-operative hemorrhage and/or thrombosis.
3. Special conditions for use statement(s):
   Prescription Use Only
4. Special instrument requirements:
   ROTEM® *delta* instrument

I. Device Description:

The ROTEM® *delta* EXTEM® reagent consists of a rabbit brain thromboplastin, heparin inhibitor, phospholipids, preservatives, and buffer. It is available as a 10 vial kit.

The ROTEM® *delta* FIBTEM® is a mixture of a platelet inhibitor (cytochalasin D) and $CaCl_2$, buffer and preservative. It is available as a 10 vial kit.

The ROTEM® *delta* APTEM® contains aprotinin, $CaCl_2$, buffer and preservative.

ROTROL N and ROTROL P consist of lyophilized plasma, fibrinogen, and buffer.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Haemoscope Corporation Thrombelastograph® Coagulation Analyzer (TEG®) 5000 Series
2. Predicate 510(k) number(s):
   k895844, k904204, k954437, k993678, k002177
3. Comparison with predicate:

EXTEM®

Similarities		
Item	Device	Predicate
Intended Use	The EXTEM 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*®. Clotting characteristics are described by the functional	The TEG - 5000 Series Analyzer is intended to be used to provide a quantitative and qualitative indication of the coagulation state of a blood sample by monitoring, measuring, analyzing and reporting coagulation parameter information. The

Similarities		
Item	Device	Predicate
	parameters Clotting Time (CT), Speed of Clot Formation (CFT and alpha angle), Clot firmness and Clot Lysis (LOT, ML, LI(x)).	Thrombelastograph (TEG) Coagulation Analyzer TEG - 5000 Series records the kinetic changes in a sample of whole blood, plasma or platelet rich-plasma as the sample clots (R or R-Time, K or K-TIME, Angle, and MA), retracts and/or lyses (breaks apart) (LY30/LY60, A30/A60, EPL, CLT, and LTE).
Activation Principle	Tissue Factor (TF)	Same
Extrinsic contact Activation Reagent	Rabbit brain thromboplastin, $CaCl_2$	Same

Differences		
Item	Device	Predicate
Sample size	300 µL citrated whole blood	360 µL citrated whole blood
Instrument	ROTEM *delta* instrument	TEG-5000 series analyzers

FIBTEM®

Similarities		
Item	Device	Predicate
Intended Use	The FIBTEM assay is a semiquantitative *in vitro* diagnostic assay on the ROTEM® *delta* Thromboelastrometry System to monitor the clot firmness of a citrated whole blood specimen after blocking platelet contribution to the clot firmness. Fib-TEM® is always used in conjunction with ex-TEM®. Clotting characteristics are described by the functional parameter Clot Firmness (A20/MCF).	The TEG - 5000 Series Analyzer is intended to be used to provide a quantitative and qualitative indication of the coagulation state of a blood sample by monitoring, measuring, analyzing and reporting coagulation parameter information. The Thrombelastograph (TEG) Coagulation Analyzer TEG - 5000 Series records the kinetic changes in a sample of whole blood, plasma or platelet rich-plasma as the sample clots (R or R-Time, K or K-TIME, Angle, and MA), retracts and/or lyses (breaks apart) (LY30/LY60, A30/A60, EPL, CLT, and LTE).
Activation Principle	Tissue Factor	Same
Reagent	Rabbit brain thromboplastin, $CaCl_2$,	Same

Differences		
Item	Device	Predicate
Platelet Blocker	Cytochalasin D	ReoPro®
Instrument	ROTEM *delta* instrument	TEG 5000 series analyzer

APTEM®

Similarities		
Item	Device	Predicate
Intended Use	The APTEM assay is a semiquantitative *in vitro* diagnostic assay on the ROTEM® *delta* Thromboelastrometry System to monitor the clot firmness of a citrated whole blood specimen after blocking hyperfibrinolysis by aprotinin. ap-TEM® is always used in conjunction with ex-TEM®. Clotting characteristics are described by the functional parameter Clot Firmness (A20/MCF)	The TEG - 5000 Series Analyzer is intended to be used to provide a quantitative and qualitative indication of the coagulation state of a blood sample by monitoring, measuring, analyzing and reporting coagulation parameter information. The Thrombelastograph (TEG) Coagulation Analyzer TEG - 5000 Series records the kinetic changes in a sample of whole blood, plasma or platelet rich-plasma as the sample clots (R or R-Time, K or K-TIME, Angle, and MA), retracts and/or lyses (breaks apart) (LY30/LY60, A30/A60, EPL, CLT, and LTE).
Activation Principle	Tissue Factor	Same
Reagent	Rabbit brain thromboplastin, $CaCl_2$,	Same
Fibrinolytic Blocker	Aprotinin	Same

Differences		
Item	Device	Predicate
Sample size	300 µL citrated whole blood	360 µL citrated whole blood
Instrument	ROTEM *delta* instrument	TEG 5000 series analyzer

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

EN ISO 13485:2003 *Medical devices – Quality management systems – Requirements for regulatory purposes* (ISO 13485:2003) German Version EN ISO 13485:2003

EN ISO 14971:2001 + A1*Medical devices – Application of risk management to medical devices* (ISO 14971:2000 + A1:2003) German Version EN ISO 14971:2001 + A1:2003

CLSI EP09-A2, *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline. (In Vitro Diagnostics)*Date of Standard: 2002

CLSI EP05-A, Vol.19, No. 2 *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline* Date of Standard: 1999

CLSI C28-A2, *How to Define and Determine Reference Intervals in the Clinical Laboratory; Approved Guideline – Second Edition. (In Vitro Diagnostics)* Date of Standard: 2000

CLSI EP07-A, Vol. 22, No. 27 *Interference Testing in Clinical Chemistry; Approved Guideline*

Guidance for Industry and FDA Staff: 510(k) Submissions for Coagulation Instruments (June 19, 2003)

Guidance for Industry and FDA Staff: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices (May 11, 2005)

L. Test Principle:

Thromboelastometry is based on the measurement of elasticity of blood by continuous graphic logging of the firmness of a blood clot during clot formation (coagulation factors and inhibitors, platelets and fibrin) and subsequent fibrinolysis.

The EXTEM assay is similar to the laboratory prothrombin time (PT) test. Calcium chloride ($CaCl_2$) and EXTEM® reagent are pipetted into the assay cup and then citrated whole blood is added and mixed. The cup is then inserted into the measurement position of the ROTEM® *delta* analyzer and the reaction is recorded. The initiation phase (clotting time = CT) is the time from test start until the formation of first significant detectable fibrin is reached. The clot formation phase (CFT) is the time from the CT until a clot firmness of 20 mm is reached. The A10 and A20, is the clot firmness at 10 and 20 minutes after CT. Maximum clot firmness (MCF) measures the maximum amplitude of the developed clot, and the alpha angle is the angle between the baseline and a tangent to the clotting curve through the 2 mm point.

The FIBTEM assay measures the fibrin contribution to clot firmness. Equal amounts of EXTEM® and FIBTEM® reagents are pipetted into the instrument sample cup, and then patient sample is added and mixed with the reagents. The cup is then inserted into the measurement position of the ROTEM® *delta* analyzer and the reaction recorded. The initiation phase (clotting time = CT) gives information on the extrinsic clotting factor concentration. The A20, MCF parameters gives information on the overall colt firmness without platelet activity.

The APTEM assay provides information (clotting time, speed of clot formation, and clot firmness) without fibrinolysis effects. Evidence of fibrinolytic activity is obtained by comparing the results of the EXTEM and APTEM test. In the APTEM assay, activation is initiated by the EXTEM® reagent via the extrinsic system in conjunction with the plasmin-antagonist Aprotinin, which prevents fibrinolysis. Fibrinolytic processes are detected by a loss of the clot firmness during the clot formation analysis with the ROTEM® *delta* in the EXTEM assay.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Total, within-run (channel-to-channel) and operator-to-operator precision were evaluated. The sample pool consisted of the following sample types:

   - Normal blood samples in the manufacturer established reference ranges
   - Level 1 blood samples at the medical decision limit between normal and hypocoagulable: normal blood samples diluted with physiologic saline solution and spiked with a direct thrombin inhibitor
   - Level 2 blood samples outside the reference ranges (at the medical decision limit between normal and hypercoagulable): normal sample spiked with fibrinogen (up to approximately 8 g/L)
   - ROTROL N (level 1 - mimicking 'normal')

- ROTROL P (level 2 - mimicking 'pathological')

Citrated whole blood samples were obtained from a blood donor center, and from these normal blood samples, the level 1 and level 2 blood samples were generated by diluting or spiking.

Within-run precision was assessed by performing five consecutive runs of each sample/control. Each run was performed using four different channels of one ROTEM® instrument in parallel which resulted in 20 replicates per test and sample.

Because the FIBTEM assay contains a platelet inhibitor, only the fibrin contribution to clot firmness is measured in the assay. Therefore, only the clot firmness parameter A20 is relevant for precision testing.

Rotrol N and Control P results were deemed acceptable if the results fell within the acceptable range for the control. Results from the Normal Donor and Level 1 & 2 Samples were deemed acceptable based on the following:

EXTEM/ FIBTEM/APTEM Acceptance Criteria

	CT CV (%)	CFT CV (%)	A-angle CV (%)	A20 CV (%)
Within-run	<10	<20	<5	<5
Between Operator	<10	<30	<5	<6

Results are summarized below:

Primary Parameters

A20 within-run precision (n=20)

	Normal Donor CV%	Level 1 CV%	Level 2 CV%	ROTROL N CV%	CONTROL P CV%
EXTEM	1.9	6.0	2.7	11	5.0
APTEM	2.7	3.3	2.5	N/A	N/A
FIBTEM	2.9	11.5	2.9	N/A	N/A

CT within-run precision (n=20)

	Normal Donor CV%	Level 1 CV%	Level 2 CV%	ROTROL N CV%	CONTROL P CV%
EXTEM	4.4	6.7	5.6	3.1	4.2
APTEM	7.8	7.1	6.2	N/A	N/A
FIBTEM*	N/A	N/A	N/A	N/A	N/A

*Only the Amplitude parameters (A10, A20, and MCF) are relevant for the FIBTEM assay.

Secondary Parameters

CFT within-run precision (n=20)

	Normal Donor CV%	Level 1 CV%	Level 2 CV%	ROTROL N CV%	CONTROL P CV%
EXTEM	5.5	19.1	34.6*	21.0*	34.5*
APTEM	7.3	9.5	15.4	N/A	N/A
FIBTEM*	N/A	N/A	N/A	N/A	N/A

*Not clinically significant. CFT is an ancillary parameter, no clinical decision based solely on CFT.

Alpha Angle within-run precision (n=20)

	Normal Donor CV%	Level 1 CV%	Level 2 CV%	ROTROL N CV%	CONTROL P CV%
EXTEM	1.4	5.3	1.2	0.6	1.7
APTEM	2.2	3.1	0.7	N/A	N/A
FIBTEM*	N/A	N/A	N/A	N/A	N/A

Total Precision

EXTEM, the activator for all three assays (EXTEM, APTEM, FIBTEM) was investigated for total precision (between-run) by analyzing ROTROL N and ROTROL P in duplicate on two separate runs, over 20 working days. The two test runs were separated by at least two hours. Results were presented using arithmetic means and the S_{wr} and S_T standard deviations. Additionally, between-day (S_{dd}) and between-run (S_{rr}) standard deviations were presented.

A20

	ROTROL N						ROTROL P					
	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T
EXTEM	80	42.2	1.3	1.3	0.7	2.0	80	24.6	0.4	0.0	0.8	0.9

CT

	ROTROL N						ROTROL P					
	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T
EXTEM	80	45.2	1.0	1.2	1.9	2.4	80	91.4	3.2	2.8	4.8	6.4

CFT

	ROTROL N						ROTROL P					
	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T
EXTEM	80	24.4	0.6	2.9	2.2	3.7	80	274.8	34.1	0.0	67.7	75.8

Alpha Angle

	ROTROL N						ROTROL P					
	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T	n	Mean	S_{dd}	S_{rr}	S_{wr}	S_T
EXTEM	80	85.9	0.1	0.0	0.4	0.4	80	75.8	0.6	0.8	1.1	1.4

Between-Operator Precision

Between-operator precision was investigated by five different operators analyzing the two control samples on one working day, using two different channels per test and sample.

	ROTROL N CV%				ROTROL P CV%			
	A20	CT	CFT	Alpha	A20	CT	CFT	Alpha
EXTEM	5.5	7.9	13.4	0.3	2.4	5.6	22.4	2.1

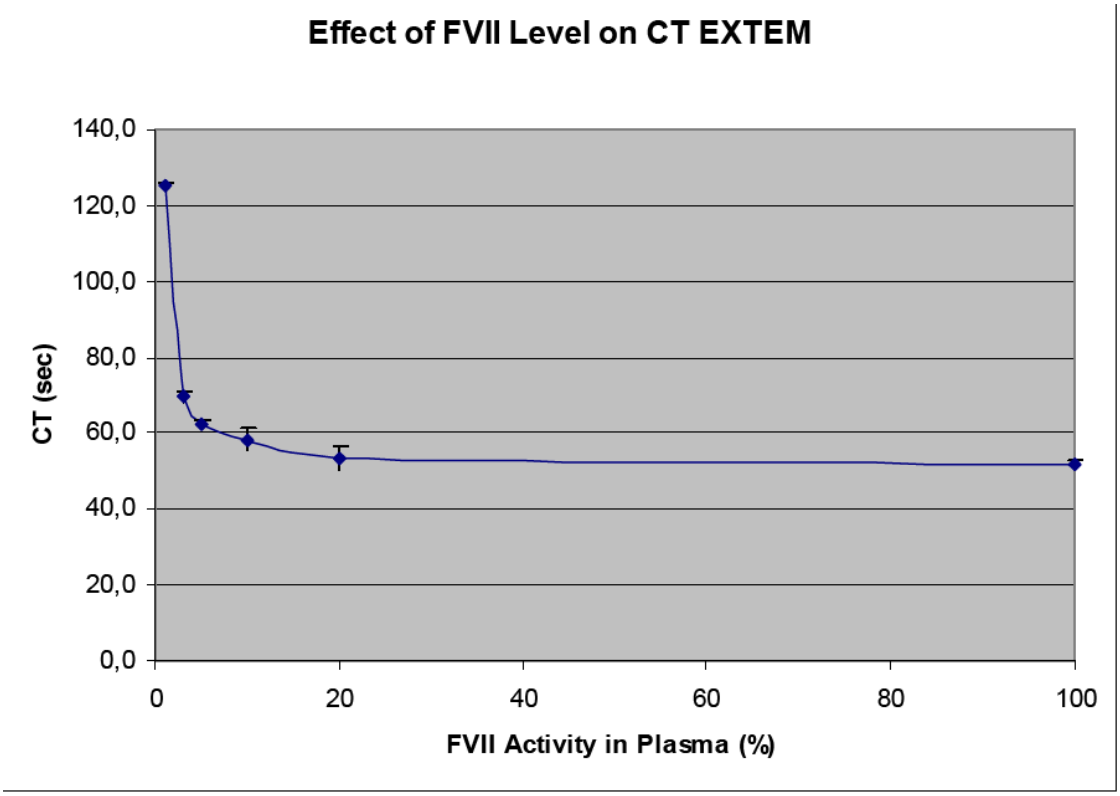
Within-Run Reproducibility

A within-run reproducibility study was conducted using 3 sites, 3 lots and 3 different instruments. ROTROL N and ROTROL P were run eight times for each lot (n=24/lot).

	ROTROL N %CV											
	Lot 1				Lot 2				Lot 3			
	CT	CFT	A20	Alpha angle	CT	CFT	A20	Alpha angle	CT	CFT	A20	Alpha angle
EXTEM	3.6	9.4	2.0	0.2	8.6	11.8	2.7	0.5	3.8	8.7	3.2	0.6

	ROTROL P %CV											
	Lot 1				Lot 2				Lot3			
	CT	CFT	A20	Alpha angle	CT	CFT	A20	Alpha angle	CT	CFT	A20	Alpha angle
EXTEM	7.2	19.7	3.5	2.5	7.0	17.1	3.2	1.9	12.4	15.2	2.7	4.2

b. Factor sensitivity to Factor VII (FVII) for the EXTEM assay was demonstrated by diluting calibration plasma (IL Calibration Plasma k041905, Factor VII level = 105%) with Factor VII deficient plasma (IL Factor VII Deficient Plasma, k024082 Factor VII level = 1%) and testing. Four aliquots of each data point were prepared, run, and the mean of the four determinations plotted against FVII concentration. Because the CT-parameter is the most sensitive signal for factor deficiency, only CT-values of the ex-TEM® reagent were estimated. Results demonstrated that Factor VII levels <20% significantly prolong the CT.



c. *Linearity/assay reportable range:*
Not applicable

d. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Data was submitted to support the 8-hour on-board and 14-day open vial stability claims for the ex-TEM, fib-TEM, and ap-TEM reagents. To support the 8-hr on board stability claim, all reagents were opened and stored at 25°C and tested at 1-hr intervals. ROTROL N was used as the sample material. Results were deemed acceptable if the ratio from the mean of the first three data points (hrs. 1-3) and the mean of the last three data points (hrs 6-8) is less than 15% for the CT parameter, CFT <25%, A20 <5% (fib-TEM <20%), and <5% for the Alpha parameter. For the 14-day stability study, reagent vials were opened, used, closed, stored at 2-8°C, and tested on days 3, 7, 10, and 14. ROTROL N was used as the sample material. All reagents have shown stability up to 14 days without any significant changes.

e. *Detection limit:*
Not applicable

f. *Analytical specificity:*
Aprotinin, tranexamic acid and epsilon-aminocaproic acid (EACA) interference were evaluated per CLSI EP7A. The three potential interferents were spiked in vitro with two concentrations (one at the highest concentration reported or three times the maximum therapeutic dose, and a lower –but still high concentration) of the antifibrinolytic substances and compared to the non-spiked interferent free control sample.

Interferent	Maximum Concentration	Lower Concentration
Aprotinin	400 KIU/mL	200 KIU/mL
Tranexamic Acid	60 µg/mL	30 µg/mL
EACA	600 µg/mL	300 µg/mL

Results showed that none of the possible interferents had an influence on the extrinsic coagulation activation up to at least twice the highest clinical dose.

Interference data for unfractionated heparin, for dilution effect, and for urokinase on the EXTEM, APTEM, and FIBTEM assays, were provided to demonstrate thromboelastograph principles: coagulation kinetics, clot firmness, and hyperfibrinolysis. Testing was conducted by testing five dilution levels of the interferent in normal blood (n=10) in parallel with the undiluted blood sample.

Heparin was spiked into citrated blood samples from blood donors in the concentrations 2, 3, 4, 5, and 8 U/mL to determine the maximum concentration which leaves the CT and MCT/A20 unaltered. Four aliquots of each heparin concentration level was prepared and assayed. The mean and SD for each concentration was presented. For the 5 and 8 U/mL aliquots, the median CT results were prolonged in comparison to the heparin free control, and were above the upper reference range limit. A similar less pronounced effect was seen on the CFT, Alpha Angle, and A20 parameters.

Sensitivity to dilution effect was presented to demonstrate clot firmness. Blood samples depleted of platelets or fibrinogen decreases clot firmness. To simulate the depletion of platelets and fibrinogen due to plasma expander substitution in a patient, normal blood was diluted in saline to 90, 80, 70, 60 and 50%. Ten different blood samples from normal donors were diluted and tested in parallel. The mean, SD, median, upper and lower quartile, min, and max over the ten samples was determined for each dilution. The median and upper and lower quartile was presented graphically (median ± quartile) by dilution. A linear reduction was seen with each dilution on all EXTEM, APTEM, and FIBTEM parameters.

Urokinase (UK), a plasmin activator was used to show a relationship between activation of plasmin and concomitant hyperfibrinolysis and the breakdown of the clot in EXTEM. UK was spiked into normal citrated blood samples in the concentrations 10, 20, 30, 40, and 50 U/mL and the EXTEM and APTEM assays were performed. Ten different blood samples from normal donors were diluted and tested in parallel. The mean, SD, median, upper and lower quartile, min, and max over the ten samples was determined for each dilution. The median and upper and lower quartile was presented graphically (median ± quartile) by dilution. Clot lysis was seen within one hour in the 20, 30, 40 and 50 U/mL concentrations for the EXTEM assays. UK did not affect any parameter of the APTEM assay, indicating that the aprotinin in APTEM assay blocks fibrinolysis.

g. Assay cut-off:

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*
Clinical samples from patients (n=78) with suspected or acute hemostasis disorders in the peri- or post-operative phase or at the ICU from 3 US sites were enrolled into the study. The study included patients with normal coagulation, hypocoagulable and hypercoagulable states in order to obtain results over the whole range of the individual parameter results. A unique sample identifier, the reason for the surgery, and a brief qualitative description of the clinical finding at the time of blood draw were obtained for each patient included in the study. The samples for the activated tests were analyzed within two hours from blood draw, the non-activated test (NATEM) was analyzed within one hour.

The EXTEM assay run on the ROTEM® *delta* was compared to a generic tissue factor reagent run on the predicate device. The FIBTEM assay run on the ROTEM® *delta* was compared to tissue factor reagent plus ReoPro® run on the predicate. The APTEM assay run on the ROTEM® *delta* was compared to the tissue factor reagent with aprotinin run on the predicate.

Due to limited blood volumes taken, not all patients were tested with all assays per protocol. At one site, 6 patients were tested at multiple time points during surgery. Data from each site was analyzed by Ordinary Least Squares and Deming regression and results demonstrated no significant difference between sites.

EXTEM
MCF vs. TEG MA

	N	**Min ROTEM®/ TEG®**	**Max ROTEM®/ TEG®**	**Slope Deming**	**Intercept Deming**	**R**
All Sites	70	36/33	80/78	0.97	0.15	0.9979
Atlanta	27	38/42	75/73	1.09	-6.55	1.0072
Durham	23	44/44	71/75	0.81	10.00	0.9852
Orlando	20	36/33	80/78	0.98	-1.25	0.9995

CT vs. TEG R

	N	**Min ROTEM®/ TEG®**	**Max ROTEM® /TEG®**	**Slope Deming**	**Intercept Deming**	**R**
All Sites	71	1/0	5/4	1.21	0.10	1.0314
Atlanta	28	1/1	2/2	2.24	-1.00	1.3019
Durham	23	1/0	2/1	1.07	0.35	1.0209
Orlando	20	1/1	5/4	1.11	0.09	1.0033

APTEM
MCF vs. TEG MA

	n	Min ROTEM®/ TEG®	Max ROTEM®/ TEG®	Slope Deming	Intercept Deming	R
All Sites	55	35/38	80/77	0.98	-0.41	0.9975
Atlanta	14	35/40	64/69	0.99	-1.15	0.9990
Durham	21	45/38	67/74	0.68	17.76	0.9425
Orlando	20	38/40	80/77	1.16	-11.98	1.0070

CT vs. TEG R

	n	Min ROTEM®/ TEG®	Max ROTEM®/ TEG®	Slope Deming	Intercept Deming	R
All Sites	55	1/0	5/4	1.52	-0.08	1.0484
Atlanta	14	1/1	4/2	2.82	-1.54	1.3533
Durham	21	1/0	2/2	1.11	0.32	1.0273
Orlando	20	1/1	5/4	1.42	-0.99	1.0074

FIBTEM
MCF vs. TEG MA

	n	Min ROTEM®/ TEG®	Max ROTEM®/ TEG®	Slope Deming	Intercept Deming	R
All Sites	65	2/3	45/47	1.11	-5.78	1.0090
Atlanta	23	2/3	44/43	1.04	-4.58	1.0024
Durham	22	8/13	45/35	1.48	-14.01	1.0459
Orlando	20	6/5	44/47	0.99	-2.87	0.9996

b. Matrix comparison:
Not applicable

3. Clinical studies:
   a. Clinical Sensitivity:
   Not applicable
   b. Clinical specificity:
   Not applicable
   c. Other clinical supportive data (when a. and b. are not applicable):
   Not applicable
4. Clinical cut-off:
   Not applicable
5. Expected values/Reference range:
   Reference ranges for the ROTEM® were determined following the CLSI C28-A2

guideline at 3 US sites (n=127 apparently healthy blood donors). The reference ranges showed no significant difference between centers or from ranges established at European sites.
Each laboratory is recommended to establish a site specific reference range.

		MCF (MM)	A20(mm)	CT(sec)	CFT(sec)	Alpha(°) ROTEM®
EXTEM	US	52-70	50-70	43-82	48-127	65-80
FIBTEM	US	7-24	7-24			
APTEM	US	52-70	50-70	43-82	48-127	65-80

N. Proposed Labeling:

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

O. Conclusion:

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