510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K220282

B Applicant

Abbott Laboratories

C Proprietary and Established Names

i-STAT PT*plus* Cartridge with i-STAT 1 System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
GJS	Class II	21 CFR 864.7750 - Prothrombin Time Test	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

Clearance of a new device

B Measurand:

Prothrombin Time (PT)
International Normalized Ratio (INR) (seconds)

C Type of Test:

Quantitative

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The i-STAT PT*plus* cartridge is intended for use in the in vitro quantitative measurement of the clot time of the extrinsic coagulation pathway when activated by thromboplastin in non-anticoagulated whole blood (venous or capillary), using the i-STAT 1 System. Measurements of prothrombin time are used to aid in the monitoring of patients receiving anticoagulant therapy with coumarin derivatives. The i-STAT PT*plus* Prothrombin Time test result is reported in seconds and as an International Normalized Ratio (INR). The test is intended for point of care use and is for prescription use only.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

i-STAT 1 analyzer (K001387)
i-STAT 1 Wireless Analyzer (K103195)

IV Device/System Characteristics:

A Device Description:

The i-STAT 1 System consists of the i-STAT 1 analyzer and the i-STAT cartridges. The i-STAT PT*plus* cartridge is a coagulation cartridge for determining the time required for complete activation of the extrinsic coagulation cascade. The cartridge contains electrochemical sensors and test reagents that must be mixed with the sample. The reagents include the reactive ingredient to activate the coagulation cascade as well as electrochemical markers that generate a sensor signal when the cascade is fully activated.

The analysis time of the i-STAT PT*plus* cartridge is up to 300 seconds or 5 minutes. The sample volume required for the i-STAT PT*plus* cartridge is approximately 20 µl of whole blood (venous or capillary) without added anticoagulant. The i-STAT PT*plus* cartridge is a single-use disposable unit that is self-contained. The test reagents and sample fluids do not contact the instrument or user. All the test steps and fluid movements occur within the cartridge.

Other components of the i-STAT 1 System are the Electronic Simulator, the i-STAT 1 Downloader/Recharger and the i-STAT Printer. The i-STAT 1 analyzer is a handheld, in vitro diagnostic analytical device designed to run only i-STAT test cartridges. The system is designed for use by trained medical professionals at the patient point of care or in the clinical laboratory and is for prescription use only. The i-STAT 1 System has an internal quality control (internal simulator) and an external quality control (Electronic Simulator). The internal and external simulators are used to check the instrument signal-reading function. In addition to the quality controls within the i-STAT 1 System, liquid quality controls are available as an optional quality control methodology to meet the regulatory compliance requirements applicable to the facility where they are to be used.

The liquid quality controls are the i-STAT PT*plus* Control Levels 1 and 2 and can be used for the quality control of the i-STAT PT*plus* cartridge. The coagulation controls consist of lyophilized citrated human plasma and calcium chloride fluid for reconstitution. i-STAT PT*plus* Control Level 1 has been formulated to produce a normal prothrombin time. Level 2 has been formulated to produce an extended prothrombin time. Each level of control is packaged as a box of 5 vials

containing 1 mL of lyophilized citrated human plasma and 5 vials of 1.5 mL of calcium chloride diluent.

The i-STAT PT*plus* controls are intended for use with the i-STAT PT *plus* cartridge on the i-STAT System, and values assigned to these controls may not be commutable with other commercial methods.

B Principle of Operation:
The i-STAT PT*plus* cartridge with the i-STAT 1 Analyzer uses electrochemical technology with amperometric (electric current) detection of thrombin activity to generate a clot time. The prothrombin time test result is reported as an International Normalized Ratio (INR) and/or in seconds.

In a prothrombin time test, coagulation is initiated by exposing the sample to tissue thromboplastin. In the i-STAT Prothrombin time test, complete activation is indicated when activated thrombin converts a thrombin substrate to fibrin and extensive or localized clots are detected by an electrochemical sensor.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Coaguchek XS Plus System

B Predicate 510(k) Number(s):
K071041

C Comparison with Predicate(s):

Device & Predicate Device(s):	K220282	K071041
Device Trade Name	i-STAT PT*plus* cartridge with the i-STAT 1 System	CoaguChek® XS Plus System
General Device Characteristic Similarities		
Intended Use/Indications For Use	The i-STAT PT*plus* cartridge is intended for use in the in vitro quantitative measurement of the clot time of the extrinsic coagulation pathway when activated by thromboplastin in non-anticoagulated whole blood (venous or capillary), using the i-	Intended for use by professional healthcare providers for quantitative prothrombin time testing for the monitoring of warfarin therapy. The system uses fresh capillary or non-anticoagulated venous whole blood.

	STAT 1 System. Measurements of prothrombin time are used to aid in the monitoring of patients receiving anticoagulant therapy with coumarin derivatives. The i-STAT PT*plus* Prothrombin Time test result is reported in seconds and as an International Normalized Ratio (INR). The test is intended for point of care use and is for prescription use only.	
Principle of Measurement	Electrochemical technology with amperometric (electric current) detection of thrombin activity	Same
Reportable Range	0.8 – 8.0 INR	0.8 – 8.0 INR
Sample Type	Fresh whole blood from venous or capillary samples	Same
Sample Preparation	Ready to use. No sample preparation required	Same
Traceability	Traceable to the WHO international reference method; rTF-16	Same
Reagent	Human recombinant thromboplastin	Same
Electronic Quality Controls	On-board quality control built into the analyzer and external Electronic Simulator	On-board quality control which uses electrochemical signal to detect test strip integrity
Liquid Quality Controls	Two levels of liquid controls	Same
Analyzer Type	Handheld	Same
Output	PT in seconds and INR	Same

General Device Characteristic Differences		
Measurement software	Results calculated from analyzer-measured parameters	Converts raw signal into PT result
Sample Volume	Approximately 20 µL	Minimum of 10 µL
Quality Control Lockout	Not available for external liquid controls	If QC result fails, the operator is locked from performing testing
Control Target Values	Lot-specific target values provided in QC package insert	Lot-specific target values provided on QC code chip

VI Standards/Guidance Documents Referenced:

- CLSI EP05: *Evaluation of Precision of Quantitative Measurement Procedures;* Approved Guideline - Third Edition
- CLSI EP28: *Defining, Establishing, and Verifying, Reference Intervals in the Clinical Laboratory*; Approved Guideline - Third Edition
- CLSI EP07: *Interference Testing in Clinical Chemistry*; Second Edition
- CLSI POCT14-ED2 *Point-of-Care Coagulation Testing and Anticoagulation Monitoring*; Second Edition
- CLSI H54; *Procedures for Validation of INR and Local Calibration of PT/INR Systems;* Approved Guideline
- CLSI EP25-A, *Evaluation of Stability of In Vitro Diagnostic Reagents;* Approved Guideline

VII Performance Characteristics:

A Analytical Performance:

1. Precision/Reproducibility:

a. 20-day Liquid Control Precision Study

A single-site precision study was performed over the course of 20 non-consecutive days, two runs per day, by two POC healthcare professionals using three lots of i-STAT PT*plus* cartridges and i-STAT PT*plus* Controls (L1 and L2) as well as an internal control fluid (L3) on 18 i-STAT 1 analyzers. The 20-day precision of the prothrombin time test in the i-STAT PT*plus* cartridge with the i-STAT 1 System has been demonstrated to be within the acceptance criteria at each control level and for each cartridge lot. The results of this study demonstrated acceptable within-laboratory precision for all three control levels.

20 Day Precision Result Summary (seconds)												
Fluid Level	N	Mean	Repeatability		Between-lot		Between-run		Between-day		Within-lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	359	10.44	0.274	2.6	0.113	1.1	0.084	0.8	0.133	1.3	0.335	3.1
L2	355	23.64	0.764	3.2	0.841	3.6	0.183	0.8	0.226	1.0	1.173	4.5
L3	339	51.77	2.329	4.5	1.530	3.0	0.644	1.2	0.96	0.8	2.887	5.9

20 Day Precision Result Summary (INR)												
Fluid Level	N	Mean	Repeatability		Between-lot		Between-run		Between-day		Within-lab	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	359	1.03	0.027	2.6	0.011	1.1	0.008	0.8	0.013	1.3	0.033	3.1
L2	355	2.34	0.076	3.2	0.083	3.6	0.018	0.8	0.022	1.0	0.106	4.5
L3	339	5.13	0.231	4.5	0.151	3.0	0.064	1.2	0.038	0.8	0.286	5.9

b. Lot-to-Lot Precision Study

A lot-to-lot precision study was performed over five days by three POC healthcare professionals using three lots of i-STAT PT*plus* cartridges and one lot of i-STAT PT*plus* Controls (L1 and L2) as well as an internal control fluid (L3). A total of 32 i-STAT 1 analyzers were used. The lot-to-lot precision of the prothrombin time test in the i-STAT PT*plus* cartridge on the i-STAT 1 System demonstrated acceptable precision, as the results are shown to be within the acceptance criteria for all levels.

Lot-to-Lot Precision Summary for Prothrombin Time (seconds)										
Control Fluid	N	Mean (sec)	Within-run		Between-day		Between-lot		Within-lab	
			SD	% CV	SD	% CV	SD	% CV	SD	%CV
L1	88	9.15	0.212	2.3	0.414	4.5	0.150	1.6	0.489	5.3
L2	86	23.72	0.743	3.1	1.010	4.3	1.022	4.3	1.617	6.8
L3	88	58.27	1.351	2.3	2.269	3.9	2.846	4.9	3.882	6.7
Lot-to-Lot Precision Summary for Prothrombin Time (INR)										
Control Fluid	N	Mean (INR)	Within-run		Between-day		Between-lot		Within-lab	
			SD	% CV	SD	% CV	SD	% CV	SD	%CV
L1	88	0.91	0.021	2.3	0.041	4.5	0.015	1.6	0.048	5.3
L2	86	2.35	0.074	3.1	0.100	4.3	0.101	4.3	0.160	6.8
L3	88	5.77	0.134	2.3	0.225	3.9	0.282	4.9	0.384	6.7

c. Instrument-to-Instrument Precision Study

An instrument-to-instrument precision study was performed over five days by two healthcare professionals using one lot of i-STAT PT*plus* cartridges and one lot of i-STAT PT*plus* Controls (L1 and L2) as well as an internal control fluid (L3). Each fluid level was tested on three i-STAT 1 analyzers with six replicates per analyzer, once per day for five days. The instrument-to-instrument precision of the prothrombin time test in the i-STAT PT*plus* cartridge on the i-STAT 1 System demonstrated acceptable precision, as the results are shown to be within the acceptance criteria for all levels.

Instrument-to-Instrument Precision Summary for Prothrombin Time (seconds)										
Control Fluid	N	Mean (sec)	Within-run		Between-day		Between-instrument		Within-lab	
			SD	% CV	SD	% CV	SD	% CV	SD	%CV
L1	90	10.26	0.209	2.0	0.034	0.3	0.031	0.3	0.031	0.3
L2	90	23.58	0.536	2.3	0.086	0.4	0.105	0.4	0.105	0.4
L3	90	53.34	0.811	1.5	0.129	0.2	0.381	0.7	0.38	0.7

Instrument-to-Instrument Precision Summary for Prothrombin Time (INR)										
Control Fluid	N	Mean (INR)	Within-run		Between-day		Between-instrument		Within-lab	
			SD	% CV	SD	% CV	SD	% CV	SD	%CV
L1	90	1.02	0.021	2.0	0.003	0.3	0.003	0.3	0.003	0.3
L2	90	2.33	0.053	2.3	0.008	0.4	0.010	0.4	0.010	0.4
L3	90	5.28	0.080	1.5	0.013	0.2	0.038	0.7	0.038	0.7

d. Operator-to-Operator Precision Study

An operator-to-operator precision was performed over five days by three POC healthcare professionals using one lot of i-STAT PT*plus* cartridges and one lot of i-STAT PT*plus* Controls (L1 and L2) as well as an internal control fluid (L3). Each control fluid level was tested by three operators with six replicates per operator, once per day for five days. The operator-to-operator precision of the prothrombin time test in the i-STAT PT*plus* cartridge on the i-STAT 1 System demonstrated acceptable precision, as the results are shown to be within the acceptance criteria for all levels.

Operator-to-Operator Precision Summary for Prothrombin Time (seconds)										
Control Fluid	N	Mean (sec)	Within-Run		Between-Day		Between-Operator		Within-Lab	
			SD	% CV	SD	% CV	SD	% CV	SD	%CV
L1	90	10.49	0.267	2.5	0.052	0.5	0.095	0.9	0.288	2.7
L2	90	24.31	0.456	1.9	0.124	0.5	0.016	0.1	0.473	1.9
L3	89	53.04	0.811	1.5	0.360	0.7	0.369	0.7	0.961	1.8

Operator-to-Operator Precision Summary for Prothrombin Time (INR)										
Control Fluid	N	Mean (INR)	Within-Run		Between-Day		Between-Operator		Within-Lab	
			SD	% CV	SD	% CV	SD	% CV	SD	%CV
L1	90	1.04	0.026	2.5	0.005	0.5	0.009	0.9	0.029	2.7
L2	90	2.41	0.045	1.9	0.012	0.5	0.002	0.1	0.047	1.9
L3	89	5.25	0.080	1.5	0.036	0.7	0.037	0.7	0.095	1.8

e. Multi-Day Precision Study

A multi-day precision study was performed at three POC sites by one POC healthcare professional per site. The study was performed using one lot of i-STAT PT*plus* Controls (L1 and L2) as well as an internal control fluid (L3) tested once per day for five days using six i-STAT PT*plus* cartridges on six i-STAT 1 Wireless Analyzers. The results of the multi-day precision study for the i-STAT PT*plus* cartridge with the i-STAT 1 System met the acceptance criterion for total precision by site and by level, with a range of 2.5–3.7 %CV for PT(seconds) and a range of 3.2–5.0 %CV for INR.

Multi-Day Precision Summary for Prothrombin Time (seconds)												
Fluid Level	N	Mean	Within-Day		Between-Day		Within-Site		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	90	1.03	0.039	3.8	0.024	2.3	0.045	4.4	0.005	0.4	0.045	4.4
L2	91	2.46	0.089	3.6	0.000	0.0	0.089	3.6	0.000	0.0	0.089	3.6
L3	90	5.36	0.170	3.2	0.071	1.3	0.184	3.4	0.000	0.0	0.184	3.4

Multi-Day Precision Summary for Prothrombin Time (INR)												
Fluid Level	N	Mean	Within-Day		Between-Day		Within-Site		Between-Site		Reproducibility	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
L1	90	10.49	0.210	2.0	0.164	1.6	0.266	2.2	0.023	0.2	0.267	2.6
L2	91	24.82	0.771	3.1	0.221	0.9	0.802	3.2	0.000	0.0	0.802	3.2
L3	90	54.12	1.708	3.2	0.712	1.3	1.851	3.4	0.000	0.0	1.851	3.4

f. Whole Blood Precision Study

Whole blood precision (repeatability) was evaluated using venous and capillary specimens at three ranges: non-therapeutic (INR 0.8 – 1.9), therapeutic (INR 2.0 – 4.5), and very high therapeutic (INR 4.6 - 8.0). The repeatability analysis was conducted using the data collected across three point of care sites from duplicate testing in both the capillary and the venous method comparison studies. The mean, pooled standard deviation, %CV and their respective 95% confidence intervals (CI) for PT in seconds and INR were calculated for each subject level. The table below summarize this data for all sites combined. All results met the acceptance criteria.

Capillary Whole Blood Precision Summary Prothrombin Time (seconds)							
Sample Range	N	Mean		SD		%CV	
		Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Non-therapeutic	58*	14.89	(14.06, 15.73)	1.414	(1.197, 1.727)	9.5	(8.0, 11.6)
Therapeutic	119*	28.51	(27.73, 29.30)	1.495	(1.327, 1.713)	5.2	(4.7, 6.0)
Very High Therapeutic	9	50.71	(42.88, 58.54)	2.109	(1.451, 3.851)	4.2	(2.9, 7.6)
Capillary Whole Blood Precision Summary Prothrombin Time (INR)							
Non-therapeutic	58*	1.48	(1.39, 1.56)	0.143	(0.121, 0.174)	9.7	(8.2, 11.8)
Therapeutic	119*	2.82	(2.74, 2.90)	0.148	(0.131, 0.169)	5.2	(4.6, 6.0)
Very High Therapeutic	9	5.02	(4.24, 5.80)	0.201	(0.139, 0.368)	4.0	(2.8, 7.3)
Venous Whole Blood Precision Summary Prothrombin Time (seconds)							
Non-therapeutic	65*	14.69	(13.95, 15.43)	1.047	(0.894, 1.263)	7.1	(6.1, 8.6)
Therapeutic	131	28.78	(27.97, 29.59)	0.660	(0.589, 0.751)	2.3	(2.0, 2.6)
Very High Therapeutic	13*	54.37	(48.44, 60.31)	0.785	(0.569, 1.264)	1.4	(1.0, 2.3)
Venous Whole Blood Precision Summary Prothrombin Time (INR)							
Non-therapeutic	65*	1.45	(1.38, 1.53)	0.109	(0.093, 0.131)	7.5	(6.4, 9.0)
Therapeutic	131	2.85	(2.77, 2.93)	0.069	(0.061, 0.078)	2.4	(2.1, 2.7)
Very High Therapeutic	13*	5.38	(3.80, 5.97)	0.088	(0.064, 0.141)	1.6	(1.2, 2.6)

*Results with outliers included

2. Linearity:
   Not applicable.

3. Analytical Specificity/Interference:

   a. Interference

The interference performance of the prothrombin time test in the i-STAT PT*plus* cartridge with the i-STAT 1 System was evaluated in the presence of potentially interfering endogenous or exogenous substances. The effect of each substance at each prothrombin time level (normal and therapeutic) was evaluated by comparing the performance of a test sample spiked to a high concentration of the substance and a control sample spiked with an equal volume of solvent. For an identified interferent, a dose-response was performed to determine the degree of interference as a function of the substance concentration. The common exogenous and endogenous interfering substances and their interference results are listed below and showed no significant interference up to the indicated concentration for all samples tested.

Substance	Maximum Test Concentration with no interference
Acetaminophen	1324 µmol/L
Acetylsalicylic Acid	3.62 mmol/L
Ascorbic Acid	342 µmol/L
Atorvastatin	750 µg/L
Unconjugated Bilirubin	684 µmol/L
Conjugated Bilirubin	475 µmol/L
Enoxaparin	2.0 IU/mL
Epsilon-aminocaproic acid	0.39 mg/mL
Fondaparinux	3.78 mg/L
Hemoglobin	10 g/L
Ibuprofen	2425 µmol/L
Prasugrel	265.5 ng/mL
Tranexamic Acid	45 µg/mL
Triglycerides	37 mmol/L
Uric Acid	1.4 mmol/L

For the identified PT test interferents chlorhexidine digluconate, daptomycin, and oritavancin, a dose-response experiment was performed.

Substance	Interference Result
Chlorhexidine digluconate	Prolonged results ≥ 9.58×10^{-4} %
Daptomycin	Prolonged results ≥ 0.22 mg/mL
Oritavancin	Prolonged results ≥ 104 mg/L

b. Factor Sensitivity

The factor sensitivity for factors FII, FV, FVII and FX was determined using samples prepared by proportionately combining pooled normal plasma, red blood cells and factor-deficient plasma with various percent (%) factor activity ranging from 20%–100%. Each factor was tested at eight factor activity levels with three cartridge lots and three replicates per lot on nine i-STAT 1 analyzers. The factor sensitivity for the i-STAT PT*plus* test was estimated to be FII (39.5%); FV (42.0%); FVII (21.5%); FX (22.0%).

c. Fibrinogen Sensitivity

Fibrinogen sensitivity was evaluated using one cartridge lot across five fibrinogen levels, 63, 80, 336, 599, and 702 mg/dL. The study demonstrated that the prothrombin time test

in the i-STAT PT*plus* cartridge with the i-STAT 1 System is insensitive to fibrinogen across a concentration range of 63–702 mg/dL.

d. Platelet Sensitivity
Platelet sensitivity was evaluated at three platelet levels (low, normal, and high). The study demonstrated that the prothrombin time test in the i-STAT PT*plus* cartridge with the i-STAT 1 System is insensitive to platelets in the range of 70,000–670,000/mm^3.

e. Hematocrit Sensitivity
The hematocrit sensitivity was evaluated by comparing the low hematocrit level (~23% packed-cell volume (PCV)) and the high hematocrit level (~55% PCV) to the nominal hematocrit level (~39% PCV) using three lots of i-STAT PT*plus* cartridges. The results of the internal study demonstrate that the prothrombin test time in the i-STAT PT*plus* cartridge on the i-STAT 1 System is insensitive to hematocrit between 24 to 54% PCV.

f. Heparin Sensitivity
Sensitivity to unfractionated heparin was evaluated at two heparin levels. The study demonstrated that the prothrombin time test in the i-STAT PT*plus* cartridge with the i-STAT 1 System is insensitive to unfractionated heparin concentrations up to 1.0 IU/mL.

g. Sensitivity for Lupus Anticoagulant
Sensitivity to lupus anticoagulant antibodies (LA) was evaluated using two levels (low and high) of positive LA and one level of negative LA (control). The study demonstrated that the prothrombin time test in the i-STAT PT*plus* cartridge with the i-STAT 1 System is sensitive to both low and high levels of lupus anticoagulant antibodies.

4. Assay Reportable Range:
The reportable range of the prothrombin time test in the i-STAT PT*plus* cartridge with the i-STAT 1 System was determined through a method comparison study by using venous and capillary whole blood specimens collected from subjects undergoing anticoagulant therapy with coumarin derivatives and from subjects who were not on anticoagulant therapy. The reportable range for prothrombin time test in the i-STAT PT*plus* cartridge with the i-STAT 1 System is 0.8–8.0 INR and 8.1–80.8 seconds.

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

Traceability
The traceability of the prothrombin time test in the i-STAT PT*plus* has been established against the World Health Organization (WHO) International Reference Preparation (IRP) of human recombinant tissue factor (RTF) using the tilt tube technique. The i-STAT PT*plus* cartridge is traceable to rTF/16.

Calibration
The i-STAT PT*plus* thromboplastin is specific for the i-STAT instrument. Calibration and ISI assignment is performed using multiple i-STAT instruments running i-STAT cartridges containing the i-STAT PT*plus* thromboplastin resulting in a factory calibrated PT test.

Controls

Liquid quality controls (i-STAT PT*plus* Control Levels 1 and 2) are available as an optional quality control methodology to meet facility regulatory compliance requirements. The controls are citrated pooled lyophilized plasma with a calcium chloride ($CaCl_2$) reconstitution solution. i-STAT PT*plus* Control Level 1 has been formulated to produce a normal/non-therapeutic prothrombin time and is designed to provide results within a range of 0.8–1.6 INR, while i-STAT PT*plus* Control Level 2 has been formulated to produce a therapeutic prothrombin time and is designed to provide results within a range of 1.7–3.5 INR. The controls are manufactured for Abbott Point of Care by Cliniqa Corporation.

In-Use (Reconstituted) Stability Study for Controls

The instructions for use for the i-STAT PT*plus* Controls specify that the control fluid components be equilibrated at room temperature for a minimum of 45 minutes to a maximum of 4 hours prior to reconstitution. The user is instructed to test the fluids immediately after reconstitution. The in-use stability of the controls was assessed by testing of i-STAT PT*plus* cartridges with of i-STAT PT*plus* Controls stored at room temperature over the range of the equilibration period specified above. An in-use stability study was conducted using nine vials from one lot of i-STAT PT*plus* Control Levels 1 and 2 on i-STAT PT*plus* cartridge lot using 60 i-STAT 1 analyzers. At each time interval, three vials of each fluid level were tested with 20 i-STAT PT*plus*/aPTT cartridges per vial on i-STAT 1 analyzers for a total sample size of 60 cartridges per test condition per fluid level. The results for the in-use stability study for the i-STAT PT*plus* Controls support that the controls are stable for four hours when stored at room temperature.

Shelf-Life Stability Study for Controls

A real-time shelf-life stability study was conducted using three lots for each level of i-STAT PT*plus* Control Levels 1 and 2 with seven i-STAT PT*plus* cartridge lots using six i-STAT 1 analyzers. Testing was performed at the beginning of the study (T= 0, corresponding to date of control lot manufacture), at three intervals throughout the duration of the intended shelf life and two intervals beyond the intended shelf life for a total of six test time points. The results for the real time stability study for the i-STAT PT*plus* Controls support a shelf-life of 12 months when stored refrigerated at 2–8°C.

i-STAT PT*plus* Cartridge Shelf-Life

Shelf-life stability study was conducted using three lots of i-STAT PT*plus* cartridges at 2-8°C and 18-30°C storage conditions. Three levels of the i-STAT PT*plus* control fluids, unaltered whole blood at normal prothrombin time and factor depleted samples to reflect therapeutic prothrombin times were tested at seven different test events: 0, 19, 60, 90, 120, 180, 210, and 240 days.

The stability results for the prothrombin time test in the i-STAT PT*plus* cartridge on the i-STAT 1 System support a shelf-life claim of 193 days (6 months) at 2-8°C and 14 days at 18-30°C.

6. Detection Limit:
   Not applicable.

7. Assay Cut-Off:
   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

A method comparison study was conducted. Venous and capillary whole blood specimens were prospectively collected from subjects undergoing anticoagulant therapy with coumarin derivates and from subjects who were not on anticoagulant therapy at three clinical sites. Both venous and capillary specimens were tested in duplicate on the i-STAT 1 Analyzer and were tested in singlicate on the Roche CoaguChek XS Plus System (K071041). Passing-Bablok regression analysis was performed for the first replicate of the i-STAT prothrombin time result versus the singlicate result from the CoaguChek.

Method Comparison Results for i-STAT PT*plus* Cartridge with i-STAT 1 System vs. CoaguChek XS System (Seconds)									
Matrix	**N**	**i-STAT 1 PT (sec) Range**	**CoaguChek PT (sec) Range**	**Correlation coefficient (r)**		**Slope**		**Intercept**	
				Estimate	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
Venous	191	8.5 – 67.9	10.8 – 84.6	0.98	0.97, 0.98	0.736	0.715, 0.757	1.352	0.708, 1.920
Capillary	153	8.6 – 61.9	11.1 – 83.7	0.97	0.96, 0.98	0.743	0.711, 0.776	1.051	0.309, 1.892

Method Comparison Results for i-STAT PT*plus* Cartridge with i-STAT 1 System vs. CoaguChek XS System (INR)									
Matrix	**N**	**i-STAT 1 INR Range**	**CoaguChek INR Range**	**Correlation coefficient (r)**		**Slope**		**Intercept**	
				Estimate	**95% CI**	**Estimate**	**95% CI**	**Estimate**	**95% CI**
Venous	191	0.8 – 6.7	0.9 – 7.0	0.98	0.97, 0.98	0.875	0.857, 0.906	0.113	0.045, 0.157
Capillary	153	0.8 – 6.1	0.8 – 7.0	0.97	0.96, 0.98	0.885	0.846, 0.923	0.104	0.009, 0.171

2. Method Comparison with Reference Device:

Venous and capillary whole blood specimens were prospectively collected from subjects undergoing anticoagulant therapy with coumarin derivates and from subjects who were not on anticoagulant therapy at three POC clinical sites. Both venous and capillary specimens were tested in duplicate on the i-STAT 1 Analyzer and citrated plasma from the venous whole blood specimens was tested in duplicate on the Sysmex CS-2500 (K172286) reference instrument using Dade Innovin reagent. Passing-Bablok regression analysis was performed for the first replicate of the i-STAT prothrombin time result versus the first replicate result from the Sysmex CS-2500.

Method Comparison Results for i-STAT PT*plus* Cartridge with i-STAT 1 System vs. Sysmex CS-2500 (seconds)						
Matrix	**N**	**i-STAT 1 PT (sec) Range**	**Sysmex PT (sec) Range**	**Correlation coefficient (r) (95% CI)**	**Slope (95% CI)**	**Intercept**
Venous	211	8.5 – 80.5	9.7 – 83.1	0.92 (0.90, 0.94)	1.037 (0.994, 1.082)	-0.591 (-1.500, 0.151)
Capillary	203	8.6 – 80.5	9.7 – 83.1	0.91 (0.88, 0.93)	1.023 (0.979, 1.070)	-0.189 (-1.052, 0.641)

Method Comparison Results for i-STAT PT*plus* Cartridge with i-STAT 1 System vs. Sysmex CS-2500 (INR)						
Matrix	**N**	**i-STAT 1 INR Range**	**Sysmex INR Range**	**Correlation coefficient (r) (95% CI)**	**Slope (95% CI)**	**Intercept (95% CI)**
Venous	211	0.8 – 8.0	0.9 – 8.1	0.92 (0.90, 0.94)	1.037 (1.000, 1.078)	0.004 (-0.079, 0.075)
Capillary	203	0.8 – 8.0	0.9 – 8.1	0.91 (0.89, 0.93)	1.022 (0.984, 1.061)	0.047 (-0.029, 0.127)

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):
   Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

i-STAT PT*plus* cartridge reference intervals were established with 154 venous and 146 capillary specimens on the i-STAT 1 analyzer. Testing was performed with three cartridge lots on the i-STAT 1 System at three clinical sites. The reference range for venous and capillary specimens combined is INR: 0.9–1.3.

Reference Range	**Venous**		**Capillary**	
	PT (sec)	**INR**	**PT (sec)**	**INR**
i-STAT PT*plus* Cartridge with i-STAT 1 Wireless	9.2–13.0	0.9–1.3	9.0–13.8	0.9–1.3

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.