510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM

A. 510(k) Number:

K173202

B. Purpose for Submission:

New device

C. Measurand:

Antithrombin activity (%)

D. Type of Test:

Quantitative chromogenic test

E. Applicant:

Sekisui Medical Co., LTD

F. Proprietary and Established Names:

CP3000 Coagulation Analyzer
Coagpia AT Reagent
Coagpia Calibrator
Coagpia Control Set

G. Regulatory Information:

1. Regulation section:

Device	Regulation Section
CP3000 Coagulation Analyzer	21 CFR 864.5425, Multipurpose system for in vitro coagulation studies
Coagpia AT Reagent	21 CFR 864.7060, Antithrombin III Assay
Coagpia Calibrator	21 CFR 862.1150 Calibrator
Coagpia Control Set	21 CFR 864.5425, Plasma, coagulation control

2. Classification:

Class II

3. Product code:

Device	Product Code
CP3000 Coagulation Analyzer	JPA
Coagpia AT Reagent	JBQ
Coagpia Calibrator	JIX
Coagpia Control Set	GGN

4. Panel:

Hematology (81)

H. Intended Use:

1. Intended use(s):

CP3000 Coagulation Analyzer
The CP3000 is a fully automated, random-access in vitro blood coagulation analyzer intended for use by healthcare professionals in the clinical laboratory. The CP3000 analyzer is designed to process plasma samples photometrically using chromogenic assays.

Coagpia AT Reagent
Coagpia AT Reagent is intended for the quantitative determination of antithrombin (AT) activity in human 3.2% citrated venous plasma. The reagent is intended for use on Sekisui CP3000 analyzers by trained laboratory personnel in clinical laboratories. For in vitro diagnostic use.

Coagpia Calibrator
The Coagpia Calibrator is intended for use as a calibration plasma for the following Sekisui coagulation assay on Sekisui CP3000 analyzers by trained laboratory personnel in clinical laboratories. For in vitro diagnostic use.

- *Coagpia AT Reagent*

Coagpia Control Set
The Coagpia Control set contains 2 levels of assayed plasma intended for the quality control of the following Sekisui coagulation assay on Sekisui CP3000 analyzers by trained laboratory personnel. For in vitro diagnostic use.

- *Coagpia AT Reagent*

2. Indication(s) for use:

Same as Intended Use(s) above

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

CP3000 Coagulation Analyzer

I. Device Description:

CP3000 Coagulation Analyzer
The CP3000 is an automated blood coagulation instrument which performs tests for specific parameters in citrated human plasma. The CP3000 system is capable of performing chromogenic assays, which allows analysis for both direct hemostasis measurements and calculated parameters. For this assay methodology, the analyzer employs two photometric detection methods: light scattering and absorbance. The light scattering method uses light emitting diodes at a wavelength of 660 nm, and the absorbance method uses a halogen lamp with filters providing wavelengths at 405, 570, and 730 nm. The analyzer components include the analyzer hardware and its controlling software (firmware), a personal computer (PC) with its user interface, result calculations, and patient data management software. The PC also provides the software to communicate with the host Laboratory Information System (LIS).

Coagpia AT Reagent
Coagpia AT Reagent is intended for the quantitative determination of antithrombin (AT) activity in human plasma on the CP3000 analyzer. R1 contains bovine Factor Xa, heparin sodium salt (porcine), buffer, surfactant and preservative. R2 contains a protease substrate N-acetyl-D-arginyl-glycyl-L-arginyl-p-nitroanilide, buffer, surfactant and preservative. Both reagents are liquid and do not require any preparation prior to use.

Coagpia Calibrator
The Coagpia Calibrator is lyophilized human plasma and is suitable for the calibration of the antithrombin activity assay using Coagpia AT Reagent on the CP3000 coagulation analyzer.

Coagpia Control Set
The Coagpia Control Set is lyophilized human plasma supplied as two levels (Level 1 Control and Level 2 Control) and is suitable for use with the antithrombin activity assay using Coagpia AT Reagent on the CP3000 analyzer.

J. Substantial Equivalence Information:

1. Predicate device name(s) and 510(k) numbers:

Predicate Device	Predicate 510(k) Number
ACL TOP 700 LAS	K160276
HemosIL Liquid Antithrombin	K062431
HemosIL Calibration Plasma	K041905
HemosIL Normal Control Assayed	K021023

Predicate Device	Predicate 510(k) Number
HemosIL Low Abnormal Control Assayed	K021024

2. Comparison with predicate:

CP3000 Coagulation Analyzer

Similarities		
Item	Device CP3000 (CTS and non-CTS)	Predicate ACL TOP 700 (CTS and non-CTS)
Intended use	The CP3000 is a fully automated, random-access in vitro blood coagulation analyzer intended for use by healthcare professionals in the clinical laboratory. The CP3000 analyzer is designed to process plasma samples photometrically using chromogenic assays.	The ACL TOP is a bench top, fully automated, random access analyzer designed specifically for in vitro diagnostic clinical use in the hemostasis laboratory for coagulation and/or fibrinolysis testing in the assessment of thrombosis and/or hemostasis. The system provides results for both direct hemostasis measurement and calculated parameters.
Interface	Touch screen operation Windows 7 Operating System	Same
Options	Available with closed tube sampling (CTS) function	Same
Analytes	Multiple	Same
Reagent Handling	• Refrigerated on board • Internal bar code sample identification	Same

Differences		
Item	Device CP3000 (CTS and non-CTS)	Predicate ACL TOP 700 (CTS and non-CTS)
Application type	• Chromogenic	• Coagulometric (turbidimetric) • Measurement Chromogenic (absorbance) measurement • Immunological measurement

Differences		
Item	Device CP3000 (CTS and non-CTS)	Predicate ACL TOP 700 (CTS and non-CTS)
Detection	Photometric • Absorbance • Light scattering	Photometric • Absorbance
Wavelengths	• 405 nm • 570 nm • 660 nm • 730 nm	• 405 nm • 671 nm
Throughput (non-CTS)	Up to 400 clotting tests/hour	Up to 330 PT and APTT tests/hour

Coagpia AT Reagent

Similarities		
Item	Device Coagpia AT Reagent	Predicate HemosIL Liquid Antithrombin
Intended use	Coagpia AT Reagent is intended for the quantitative determination of antithrombin (AT) activity in human 3.2% citrated venous plasma. The reagent is intended for use on Sekisui CP3000 analyzers by trained laboratory personnel in clinical laboratories. For in vitro diagnostic use.	HemoslL Liquid Antithrombin is an automated chromogenic assay for the quantitative determination of Antithrombin in human citrated plasma as an aid in the diagnosis of hereditary and acquired Antithrombin deficiency and to monitor Antithrombin substitution therapy. This in vitro diagnostic test is based on a synthetic chromogenic substrate and on Factor Xa inactivation. As a consequence, it is specific and not influenced by Heparin Cofactor II. Antithrombin levels in patient plasma are measured automatically on IL Coagulation Systems.
Analyte	Antithrombin	Same
Reagent State	Liquid, ready to use	Same
Method	Chromogenic	Same
Detection	Photometric	Same

Differences		
Item	Device Coagpia AT Reagent	Predicate HemosIL Liquid Antithrombin
Key Components	Factor Xa (bovine) Heparin N-Acetyl-D-arginyl-glycyl-L-arginyl- p-nitroanilide dihydrochloride (chromogenic substrate)	Factor Xa (bovine) Heparin N-α-Z-D-Arg-Gly-Arg-pNA·2HCl (chromogenic substrate)
Sample Type	Human citrated plasma	Human citrated plasma
Expected Values	89–131%	83−128%
Repeatability	0.7–2.9%	2.2–7.4%
Within Laboratory Precision	1.1–5.8%	3.1–8.6%
Linearity	14–140%	10–150%
Clinical reportable range	14–150%	10–150%

Coagpia Calibrator

Similarities		
Item	Device Coagpia Calibrator	Predicate HemosIL Calibration Plasma
Intended use	Coagpia Calibrator is intended for use as a calibration plasma for the following Sekisui coagulation assay on Sekisui CP3000 analyzers by trained laboratory personnel in clinical laboratories. For in vitro diagnostic use. • Coagpia AT Reagent	HemosIL Calibration plasma is intended for the calibration of coagulation assays on IL and ELECTRA Coagulation Systems. Used for the determination of PT, Fibrinogen, Single Factors, von Willebrand Factor, Antithrombin, Plasminogen, Plasmin Inhibitor, Protein C, Protein S, and as a reference plasma for APTT and TT.
Format	Lyophilized	Same
Key Components	Human plasma	Same

Differences		
Item	Device Coagpia Calibrator	Predicate HemosIL Calibration Plasma
Calibrator Type	Antithrombin	Fibrinogen, Antithrombin, PT, Single Factors, von Willebrand Factor, Plasminogen, Plasmin

Differences		
Item	Device Coagpia Calibrator	Predicate HemosIL Calibration Plasma
		Inhibitor, Protein C, Protein S, and as a reference plasma for APTT and TT.

Coagpia Control Set

Similarities			
Item	Device	Predicate	
	Coagpia Control Set	HemosIL Normal Control Assayed	HemosIL Low Abnormal Control Assayed
Intended Use	The Coagpia Control set contains 2 levels of assayed plasma intended for the quality control of the following Sekisui coagulation assay on Sekisui CP3000 analyzers by trained laboratory personnel. • Coagpia AT Reagent	HemosIL Normal Control ASSAYED is intended for the quality control of coagulation assays in the normal range on IL Coagulation and ELECTRA Systems. The normal control is prepared using human citrated plasma from healthy donors. Values for all analytes are within the normal range.	HemosIL High Abnormal Control ASSAYED is intended for the quality control of coagulation assays in the high abnormal range on IL Coagulation and ELECTRA Systems. The High Abnormal Control is prepared using human citrated plasma from healthy donors (not heparinized plasma or plasma samples under oral anticoagulation therapy) and modified to stimulate an abnormal coagulation sample. Values for all analytes are in the high abnormal range.
Format	Lyophilized	Same	Same
Key Components	Human plasma	Same	Same

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

CLSI EP05-A3, *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition*

CLSI EP15-A3, *User verification of precision and estimation of bias;* Approved Guideline-Third Edition.

CLSI EP07-A2, *Interference Testing in Clinical Chemistry;* Approved Guideline-Second Edition.

CLSI EP17-A2, *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures;* Approved Guideline—Second Edition.

CLSI EP25-A, *Evaluation of Stability of In Vitro Diagnostic Reagents;* Approved Guideline.

CLSI EP28-A3c, *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory;* Approved Guideline-Third Edition.

CLSI H21-A5, *Collection, Transport, and Processing of Blood Specimens for Testing Plasma-Based Coagulation Assays and Molecular Hemostasis Assays*.

CLSI C56-A *Hemolysis, Icterus, and Lipemia/Turbidity Indices as Indicators of Interference in Clinical Laboratory Analysis*.

L. Test Principle:

Antithrombin concentration is determined by incubating plasma with an excess of bovine Factor-Xa (FXa) in the presence of heparin. The heparin binds to and causes a conformational change in the structure of antithrombin significantly increasing its inhibitory activity. This results from the AT/heparin complex binding to FXa, forming an inactive complex (AT/heparin/FXa). The chromogenic substrate specific for FXa is then added and any residual FXa cleaves the substrate which results in a color change of the substrate. Since the residual activity of FXa reflects the activity of antithrombin, the antithrombin activity of a sample can be determined by colorimetric measurement of released p-nitroaniline (pNA) on the CP3000 analyzer.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

   The repeatability of the Coagpia Antithrombin (AT) Assay, Calibrator and Control were evaluated on three CP3000 coagulation analyzers according to CLSI EP05-A3 guideline.

For the repeatability study, three lots of the Coagpia AT reagents were tested on three instruments. For each lot of reagent, the same set of six levels of human citrated plasma covering the AMR were tested. Each sample run, was tested in duplicate with two runs per day for 20 non-consecutive days. Within-run, between-run, between-lot, between-day, between-instrument and total precision were calculated. The pre-defined acceptance criteria for within-run, between-run, between-lot, between-day, and between-instrument were met.

Reproducibility:

A multi-site precision study was performed on the CP3000 analyzer at three sites. Six-levels of citrated plasma samples covering the AMR were tested in three replicates per run with two runs per day for five non-consecutive days. Three lots of reagents was tested across three testing sites on three CP3000 analyzers, for a total of N=270 replicates for each level tested. Within-run, between-run, between-lot, between-day, within-site, between-site, and total precision were calculated. All results met the pre-defined acceptance criteria.

Sample	Mean	Between-Lot		Within-Run		Between-Run		Between-Day		Within-Site*		Between-Site		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Level 1	30.0	0.00	0.0%	1.15	3.8%	1.33	4.4%	0.37	1.2%	1.79	6.0%	1.38	4.6%	2.26	7.5%
Level 2	51.7	0.00	0.0%	1.00	1.9%	1.20	2.3%	0.36	0.7%	1.60	3.1%	1.23	2.4%	2.02	3.9%
Level 3	77.5	0.00	0.0%	0.86	1.1%	1.01	1.3%	0.00	0.0%	1.33	1.7%	0.58	0.8%	1.45	1.9%
Level 4	102.8	0.23	0.2%	0.98	1.0%	0.85	0.8%	0.00	0.0%	1.30	1.3%	0.55	0.5%	1.43	1.4%
Level 5	122.7	0.06	0.0%	1.03	0.8%	0.83	0.7%	0.00	0.0%	1.33	1.1%	0.30	0.2%	1.36	1.1%
Level 6	145.3	0.00	0.0%	2.01	1.4%	1.74	1.2%	0.54	0.4%	2.71	1.9%	1.43	1.0%	3.06	2.1%

* Within-Site is a total of Between-Day, Between-Run, and Within-Run variances.

b. Linearity/assay reportable range:

Linearity

A linearity study was conducted with three lots of Coagpia AT Reagent on the CP3000 analyzer. High antithrombin (AT) concentration plasma was diluted with AT deficient plasma to create a total of 12 samples covering the concentration of the pre-specified linearity range for AT. The linearity samples were tested with Coagpia AT Assay in quadruplicate. For each sample, deviation between the linear regression model (predicted value from 1st order regression) and the best fitting polynomial regression model was calculated. Linearity was achieved through polynomial regression. The results showed that the linearity of all three lots of Coagpia Antithrombin reagent met the pre-determined design goal of 20–135%. The linear range for the Coagpia AT assay was determined to be 14–140 %.

Reportable Range/Clinical Reportable Range

A reportable range study was conducted to determine the upper limit of the measurable range of the assay. The Auto Dilution (auto-rerun as defined in the system

software) function was turned on for this study. High AT plasma (pooled plasma) was diluted with AT deficient plasma to create the sample concentration required for this evaluation. Twelve samples within 12 different dilution ratios were measured in quadruplicate using three lots of Coagpia AT Reagent. Percent difference (Recovery) to the theoretical value was calculated for each measurement result. The data supported the design goal of 150%. Lower limit of 14% has been determined by the result of lower limit of the linearity. Therefore, the reportable range for the Coagpia Antithrombin assay is 14–150%.

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

Traceability and Value Assignment:

Coagpia Calibrator:
The Coagpia Calibrator is a calibrator with assigned values traceable to the WHO 3rd International Standard for Antithrombin Plasma NIBSC code 08/258. The values of the WHO international standards for antithrombin are transferred to an in-house primary reference standard. Routine batches of Coagpia Calibrator are value assigned for antithrombin from the in-house primary reference standard. Therefore, all lots of Coagpia Calibrator are traceable to the WHO international standards described above.

Coagpia Control Set
The Coagpia Control Set are the control materials which have assigned values traceable to the WHO 3rd International Standard for Antithrombin Plasma NIBSC code 08/258.

Stability:

On-Board Stability for Reagents
Three lots of AT reagents were evaluated for on-board stability on the CP 3000 analyzer. In this study, four citrated human plasma samples at AT concentrations of 30%, 80%, 100% and 150% were tested at the indicated time points (0, 18, 43, 66 and 90 hours). The results from all evaluations performed during this study were successful and met the pre-defined acceptance criteria. The data support 66 hours of on-board stability for the Coagpia AT reagent.

Opened-Vial Capped Stability for Reagents
Three lots of AT reagents were evaluated for opened-vial capped stability (2–8°C) on the CP 3000 analyzer. AT reagents were loaded on the CP3000 analyzer and were capped after 2 hours on board the analyzer. Reagents were then placed in the refrigerator (2–8°C) until the test day. Four citrated human plasma samples at AT concentrations of 30%, 80%, 100% and 150% were tested at the indicated time points (0, 15 29, 46, 60 and 71 days). The results from all evaluations performed during this study were successful and met the pre-defined acceptance criteria. The data support 60 days of opened-vial capped stability for the Coagpia AT reagent.

Accelerated Stability for Reagents

Three lots of Coagpia AT reagents were used to determine the accelerated stability. Reagents from each lot were kept in incubators at 31°C, 37°C and 45°C for the accelerated stability. At the indicated time points (4, 9, 16, 22, and 27 days), the Coagpia AT reagents were removed from the incubators and evaluated by testing four citrated human plasma samples at AT concentrations of 30%, 80%, 100% and 150% after each calibration. The results met the pre-defined acceptance criteria, and support the shelf-life claim of 2 years at 2–8°C.

Real-time Stability for Reagents

Three lots of Coagpia AT reagents were used to determine real-time stability. The reagents from each lot were kept at 2–8°C. At the indicated time points (0, 3, 7, 13, 19, 24, and 25 months), the Coagpia AT reagents were removed from the incubators and evaluated by testing four citrated human plasma samples at AT concentrations of 30%, 80%, 100% and 150%. The real-time stability study has been completed up to 8 months for the Coagpia AT Reagent, and support a 7-month real-time stability claim.

Transportation Stability for Reagents

One lot of Coagpia AT reagent was used to evaluate transportation stability. The reagents were stored for 5 days at 10–12°C and 5 days at 1.8–2.2°C to simulate different shipping temperatures. After the incubation, reagents were stored at 2–8°C at each time point. At the indicated time (0, 3, 7, 13, 19, 24, and 25 months), the Coagpia AT reagents were removed from the incubators and evaluated by testing four citrated human plasma samples at AT concentrations of 30%, 80%, 100% and 150%. The real-time study has been completed up to 8 months for Coagpia AT Reagent. The data supports 7 months of real-time stability for Coagpia AT reagents.

Real-time Stability and Transportation Stability for Coagpia Calibrator and Coagpia Controls

Real-time stability testing and transportation testing for the Coagpia Calibrator and Coagpia Controls were conducted in a similar manner to that of the Coagpia AT reagents. The real-time stability study and transportation stability has been completed up to 13 months for Coagpia Calibrator and Coagpia Controls. The data supports 7 months of real-time stability for Coagpia Calibrator and Coagpia Controls.

Sample Stability (at room temperature)

Sample stability study using Coagpia AT Reagent on CP3000 analyzer was conducted for fresh plasma samples stored at room temperature. Forty-three fresh plasma samples were tested in quadruplicate within an hour of specimen collection in a vacuum blood collection tube. The remaining samples were recapped and stored at room temperature (18–25ºC), and tested in quadruplicate at 2, 4, 6, 8, 24 and 26 hours after collection. For each time point, results were compared to the respective baseline (zero (0) hour) result. The data at each time point met the acceptance criteria. The data support a citrated plasma sample stability claim of 4 hours at room temperature for the Coagpia AT Reagent on the CP3000 analyzer.

Fresh/frozen Stability

To validate the fresh/frozen sample stability claim on the CP3000 analyzer with the Coagpia AT reagent, 60 plasma samples covering the linear range for the antithrombin assay were frozen in aliquots at -20°C and -80°C within 4 hours of collection. Time points tested for the -20°C and -80°C samples included day 0 (baseline), 2 weeks, 3 weeks and day 0 (baseline), 4 months, 6 months and 7 months, respectively. For each time point, samples were run in duplicate. The data support that plasma samples stored at -20°C and -80°C are stable up to 2 weeks and 6 months, respectively.

d. Detection limit:

Limit of blank (LoB) was determined using five analyte-free samples. Samples were measured in quadruplicate using three lots of Coagpia AT Reagent on two CP3000 analyzers over four days, with one LoB test conducted per day. Results were processed and analyzed following CLSI Guideline EP17-A2. The limit of blank was determined to be 3%.

Limit of detection (LoD) was determined using five analyte-free samples and five natural plasmas at concentrations near the lower limit of reportable range. These samples were measured in quadruplicate using three lots of Coagpia AT Reagent on two CP3000 analyzers over four days, with one run tested per day. Results were processed and analyzed following CLSI Guideline EP17-A2. The limit of detection was determined to be 5%.

The limit of quantitation (LoQ) of the Coagpia AT reagent was determined using five citrated plasma samples with AT concentration at approximately 11%, 13%, 15%, 17% and 19%. These samples were tested with three lots of the Coagpia AT reagent on the two CP3000 analyzers over four days, with one run tested per day. The pre-defined total error goal was met for the LoQ study.

The results for LoB, LoD and LoQ are summarized below.

LoB, LoD and LoQ		
LoB	LoD	LoQ
3%	5%	11%

e. Analytical specificity:

Interference study

Three lots of Coagpia AT reagent were evaluated for interferences on the CP3000 analyzer. In this study, four citrated human plasma samples (30%, 80%, 100% and 150%) were spiked with various concentrations of interferents and tested. Each spiked sample was tested in quadruplicate on the CP3000 analyzer.

The common endogenous and exogenous interfering substances and their interference results are listed below and showed no significant interference up to the indicated

concentration for all tested citrated plasma samples.

Endogenous Substances	
Interferent	Concentration
Triglycerides	2000 mg/dL
Unconjugated Bilirubin	100 mg/dL
Conjugated Bilirubin	100 mg/dL
Hemoglobin	700 mg/dL
α-2 Macroglobulin	500 mg/dL
α-1 Antitrypsin	600 mg/dL

Exogenous Substances	
Interferent	Concentration
Bivalirudin	30 µg/mL
Argatroban	2500 ng/mL
Dabigatran	1000 ng/mL
Rivaroxaban	25 ng/mL
Unfractionated Heparin	8.0 IU/mL
Low Molecular Weight Heparin	8.0 IU/mL

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies at three clinical sites to compare the performance of the Coagpia AT reagent on the CP3000 analyzer to the predicate device (HemosIL Liquid Antithrombin on the Instrumentation Laboratories (IL) ACL TOP 700). Additional plasma samples were obtained from three additional sites in order to achieve the desired number of samples to span the clinical reportable range. A total of 482 samples were analyzed of which 116 were fresh and 366 were frozen samples. All samples were collected in 3.2% sodium citrate anticoagulant and tested in singlet with both methods (candidate and predicate). Patient sample demographics included 218 females, aged from neonate to 95 years old, and 186 males, aged from neonate to 83 years old. Of the 482 samples, 92 samples were pediatric samples.

Deming (orthogonal) regression and ordinary linear regression (OLR) were used to determine Pearson's correlation coefficient (r), slope and intercept along with their 95% CIs were provided. Bias was determined based on the Deming regression model. The calculated bias along with its 95% CI were reported for the lower quartile, upper quartile and medical decision points (MDP). All results were within the pre-defined acceptance criteria.

Regression	Sample range	N	Slope (95% CI)	Intercept (95% CI)	R
Deming	20–140%	482	1.012 (1.000, 1.024)	0.4 (-0.8, 1.5)	0.9909
OLR	20–140%	482	1.002 (0.990, 1.015)	1.2 (0.0, 2.3)	0.9909

Bias Summary for all samples (N=482)

	Level	Predicted Recovery (95% CI)	Bias (95% CI)
Midpoint, lower quartile	46	46.9 (46.2, 47.6)	2.0% (0.4, 3.5)
MDP	70	71.2 (70.7, 71.6)	1.7% (1.0, 2.3)
MDP	89	90.4 (90.0, 90.8)	1.6% (1.1, 2.0)
Midpoint, upper quartile	133	134.9 (134.3, 135.6)	1.4% (1.0, 2.0)

b. Equivalence Studies

Matrix comparison:
A matrix comparison study was conducted to demonstrate equivalence between fresh and frozen citrated plasma samples. The study was conducted in one clinical site, using one CP3000 analyzer, three reagent lots and one calibrator lot. Sixty fresh samples covering the reportable range were measured on the CP3000 analyzer within 4 hours after blood collection. The frozen time points included 2 and 3 weeks of storage with up to two freeze/thaw cycles at -20°C and 4 months of storage with up to four freeze/thaw cycles at -80°C. Results were analyzed using Passing-Bablok regression, Pearson correlation coefficient and Bland-Altman plots. The study results demonstrated comparability between fresh and frozen samples and met the pre-defined acceptance criteria for all applicatons.

Open tube vs. Closed tube sampling (CTS) mode
The purpose and scope of this study was to demonstrate the equivalence of the testing results obtained from capped and uncapped blood collection tubes using CP3000 with CTS mode. The assay was performed first on the capped tube then on the same tube, uncapped. Sixty-four plasma samples covering the reportable range of the AT assay on the CP3000 analyzer were used to conduct this study. Three CP3000 instruments were used in this study. The results from the three CP3000 analyzers were compared. The study results demonstrated comparability between the data sets.

Closed tube sampling (CTS) instrument vs. Non-CTS
The purpose and scope of this study was to demonstrate the equivalence of the test

results obtained using CP3000 instrument models CTS versus Non-CTS. One hundred and twenty frozen plasma samples covering the reportable range of the AT assay was used to conduct the study. Each sample was aliquoted into six sample cups. The samples were measured in singlicate on CP3000 instruments (three CP3000 with CTS and three CP3000 without CTS) over three days. The performance between the two CP3000 analyzer models, CP3000 analyzer with the option of CTS capability and CP3000 analyzer without CTS capability was determined to be equivalent.

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. Reference range:

   Adult reference range
   The reference interval studies were conducted at three clinical sites in the U.S. at different geographic locations to reflect the U.S. population. Citrated plasma samples were obtained from 179 apparently healthy individuals ≥ 21 years with no current or recent history of a bleeding disorder or unexpected extended bleeding episodes. Results from all sites were pooled and all reference intervals were established by calculating the non-parametric 95% confidence interval (2.5^{th} to 97.5^{th} percentiles). The calculated normal reference range for the Coagpia AT assay is 89% to 131%.

   Pediatric reference range:
   The pediatric reference range was calculated based on the data provided in the method comparison study. These values were supported by peer reviewed literature[1].

[1] Toulon et. al., Age dependency of coagulation parameters in pediatric populations, Thrombosis and Haemostasis 116 (1): 9-16, 2016

Range	15 days to 4 weeks	1 to 5 months	6 to 11 months	1 to 5 years	6 to 10 years	11 to 17 years
Calculated Coagpia AT	33–63%	29–121%	63–122%	61–129%	64–137%	69–137%

N. Instrument Name:

CP3000 Coagulation Analyzer

O. System Descriptions:

1. Modes of Operation:

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

   Yes ___X_____ or No _____

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

   Yes _____ or No ____X____

2. Software:

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

   Yes _____X___ or No _____

3. Specimen Identification:

   Manual entry and barcode reader

4. Specimen Sampling and Handling:

   Instrument available with and without cap piercing capabalities.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

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

R. Conclusion:

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