



Food and Drug Administration
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December 12, 2016

Siemens Healthcare Diagnostics Products GmbH
Petra M. Dissmann, Ph.D.
Regulatory Affairs Manager
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Re: K162420

Trade/Device Name: Sysmex[®] CS-5100
Coagulation Factor V Deficient Plasma
Coagulation Factor II, VII and X Deficient Plasmas
Protein C Reagent
Berichrom[®] Protein C

Regulation Number: 21 CFR 864.5425

Regulation Name: Multipurpose system for in vitro coagulation studies

Regulatory Class: Class II

Product Code: JPA, GGP, GJT

Dated: September 12, 2016

Received: September 13, 2016

Dear Dr. Dissmann:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address

<http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely,

Leonthena R. Carrington -S

Leonthena R. Carrington, MS, MBA, MT(ASCP)
Director

Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological
Health

Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K162420

Device Name

Sysmex® CS-5100, Coagulation Factor V Deficient Plasma, Coagulation Factor II, VII and X Deficient Plasmas, Protein C Reagent, Berichrom® Protein C

Indications for Use (Describe)

Sysmex® CS-5100:

The Sysmex® CS-5100 is a fully automated blood coagulation analyzer intended for in vitro diagnostic use using plasma collected from venous blood samples in 3.2% sodium citrate tubes to analyze clotting, chromogenic and immunoassay methods in the clinical laboratory.

For determination of:

- Prothrombin Time (PT) seconds and PT INR with Dade® Innovin®
- Activated Partial Thromboplastin Time (APTT) with Dade® Actin® FSL
- Fibrinogen (Fbg) with Dade® Thrombin Reagent
- Coagulation Factor V with Dade® Innovin®
- Coagulation Factor VII with Dade® Innovin®
- Protein C with Protein C Reagent
- Antithrombin (AT) with INNOVANCE® Antithrombin
- Protein C with Berichrom® Protein C
- D-dimer with INNOVANCE® D-Dimer

The performance of this device has not been established in neonate and pediatric patient populations.

Coagulation Factor V Deficient Plasma:

In vitro diagnostic reagent for the determination of the activity of coagulation factor V in human plasma.

Coagulation Factor II, VII and X Deficient Plasmas:

In vitro diagnostic reagents for the determination of the activity of coagulation factor II (prothrombin), coagulation factor VII and coagulation factor X in human plasma by coagulometric methods.

Protein C Reagent:

Protein C Reagent is a coagulation test for the quantitative determination of protein C activity in human plasma.

Berichrom® Protein C:

For the quantitative determination of functionally active protein C using a chromogenic substrate as an aid in the diagnosis of inherited and acquired deficiencies.

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.

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510(k) Summary

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of 21 CFR §807.92 and follows the FDA guidance 'The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]', issued July 28, 2014.

1 Submitter

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Date Prepared: August 29, 2016

2 Device

Name of Device: Sysmex® CS-5100
Common or Usual Name: Automated Coagulation Instrument
Classification Name: Multipurpose system for in vitro coagulation studies
(21 CFR 864.5425)
Regulatory Class: Class II
Product Code: JPA
510(k) Review Panel Hematology

3 Predicate Device

Name of Device: Sysmex® CA-1500 (K011235)
Common or Usual Name: Automated Coagulation Instrument
Classification Name: Multipurpose system for in vitro coagulation studies
(21 CFR 864.5425)
Regulatory Class: Class II
Product Code: JPA
510(k) Review Panel Hematology

The predicate has not been subject to a design-related recall for any of the applications associated with this premarket notification. No reference devices were used in this submission.

Reagent Applications that are the subject of this 510(k) notification					
Application Intended Use	510(k) Number related to application on predicate device	Regulation Number	Regulatory Class	Product Code	Panel
Coagulation Factor V with Dade® Innovin® <i>In vitro diagnostic reagent for the determination of the activity of coagulation factor V in human plasma.</i>	K993299	864.7290	Class II	GJT	Hematology
Coagulation Factor VII with Dade® Innovin® <i>In vitro diagnostic reagents for the determination of the activity of coagulation factor II (prothrombin), coagulation factor VII and coagulation factor X in human plasma by coagulometric methods.</i>	K993299	864.7290	Class II	GJT	Hematology
Protein C with Protein C Reagent <i>Protein C Reagent is a coagulation test for the quantitative determination of protein C activity in human plasma.</i>	K000649	864.7290	Class II	GGP	Hematology
Protein C with Berichrom® Protein C <i>For the quantitative determination of functionally active protein C using a chromogenic substrate as an aid in the diagnosis of inherited and acquired deficiencies.</i>	K001645	864.7290	Class II	GGP	Hematology

4 Device Description / Test Principle

The Sysmex® CS-5100 is an automated blood coagulation instrument which can analyze samples using clotting, chromogenic and immunoassay methods. Analysis results are displayed on the Information Processing Unit (IPU) screen. They can be printed on external printers or transmitted to a host computer. Sold separately from the instrument are the associated

- Reagents
- Controls
- Calibrators
- Consumable materials

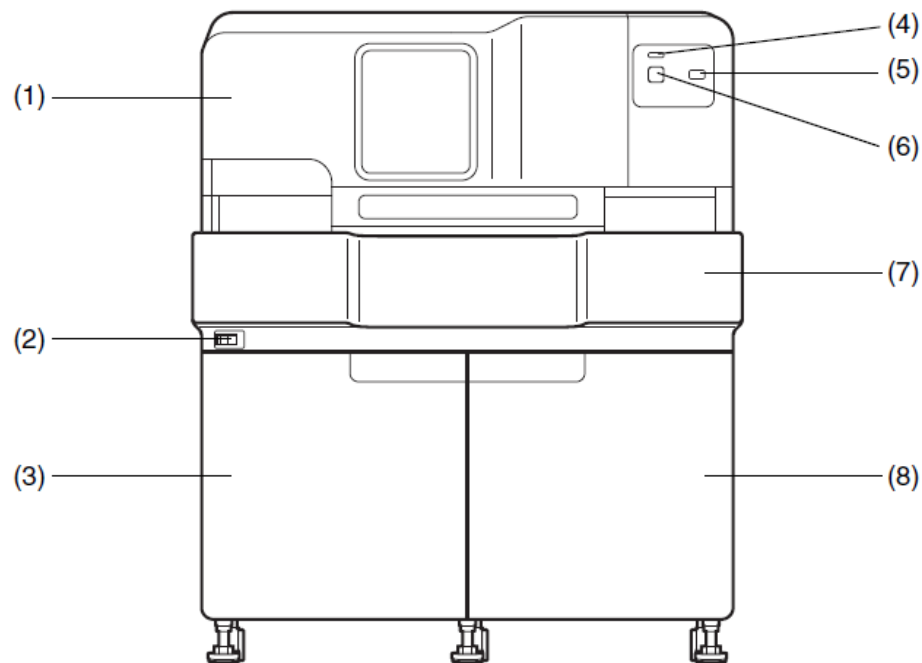
The subject of this 510(k) notification are reagent applications which perform the coagulation tests Coagulation Factor V with Dade® Innovin®, Coagulation Factor VII with Dade® Innovin®, Protein C with Protein C Reagent and Protein C with Berichrom® Protein C.

The analysis principles used on the instrument are reflected by the reagent application testing provided in this 510(k) notification and is described in the below table.

Table of Sysmex® CS-5100 Analysis Principles		
Reagent	Application	Methodology
Dade® Innovin® with Coagulation Factor V Deficient Plasma	Coagulation Factor V with Dade® Innovin®	Clotting (extrinsic pathway)
Dade® Innovin® with Coagulation Factor VII Deficient Plasma	Coagulation Factor VII with Dade® Innovin®	Clotting (extrinsic pathway)
Protein C Reagent	Protein C with Protein C Reagent	Clotting
Berichrom® Protein C	Protein C with Berichrom® Protein C	Chromogenic

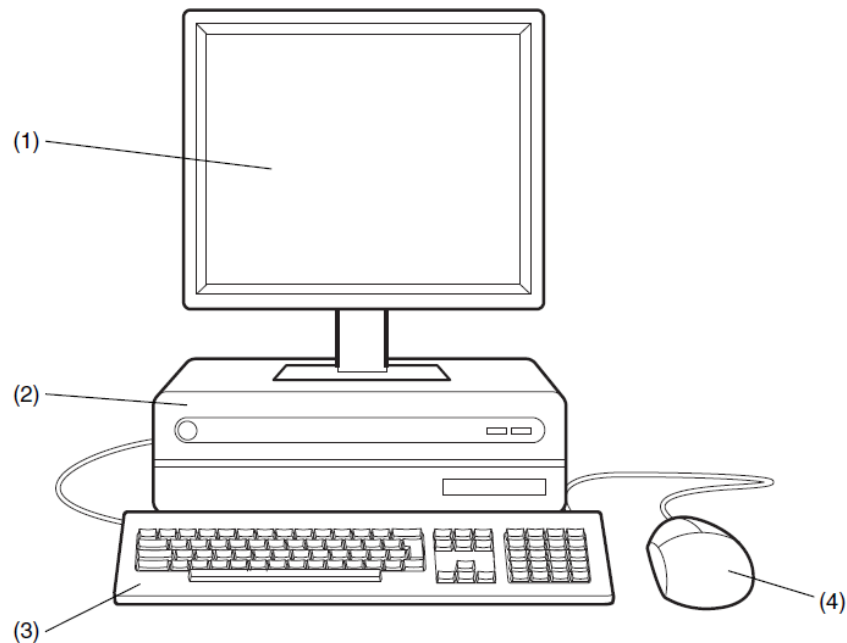
The intended Environment of Use is a clinical central/hospital laboratory.

Front View of the Instrument



- (1) Light shield lid: Open this cover to set reagents, perform maintenance, etc.
- (2) Power switch: Turns the power ON/OFF.
- (3) Left door: Holds the Pneumatic Unit inside. Open this door to adjust the positive pressure (0.22 MPa).
- (4) Alarm indicator LED: Indicates the instrument status.
- (5) Mechanical stop switch: Press this switch to immediately stop the instrument's mechanical movement.
- (6) Start button: Press this button to immediately start an analysis. This button is the same as the [Start] button on the IPU toolbar.
- (7) Sampler: Automatically transports samples that are set in the sample rack to the aspiration position.
- (8) Right door: Open the door for maintenance or to discard cuvettes.

Informational Processing Unit



- (1) Touch panel display: Displays the IPU screen. It can also be used as a touch panel.
- (2) IPU Main Unit: This is the Main Unit of IPU.
- (3) Keyboard: Used to operate the IPU together with the touch panel.
- (4) Mouse: Used to operate the IPU together with the touch panel.

Options and Accessories

Options and accessories that can be used for this instrument are as follows:

- (1) Waste tank (with float switch for waste tank): Waste fluids discharged from the Main Unit enter this tank.
- (2) Wand barcode reader: Reads barcodes to input sample numbers, rack numbers and reagent IDs.
- (3) 2D barcode reader: Reads barcodes to input calibrator's or reagent's assay sheet values, normal values and ISI values, and control's targets/limits.
- (4) IPU cart: The IPU (which includes the keyboard, PC and touch panel display), and the tanks for waste, rinse and CA Clean II can be placed on this cart.
- (5) External indicator light: The status of the instrument is indicated with a red, yellow or green light that can be seen when the operator is not directly in front of the instrument.
- (6) IPU holder: This is an optional holder for the IPU which includes the keyboard, PC and touch panel display which can be installed on the right side of the instrument to minimize the instrument footprint.

The instrument is capable of measuring in the following analysis modes:

- (1) Normal mode: Samples for all the analyses including re-analyses are taken into the instrument at the same time and analyzed. In a normal mode, a capped sample tube analysis can be performed. Automatic re-analysis can also be performed.
- (2) Micro-sample mode: Samples set in the sampler or STAT holder are taken into the instrument for each analysis through a secondary dispensing sample probe. When measurements are to be performed in Micro mode, sample tubes must be uncapped. The instrument detects capped tubes automatically and displays an error message. This analysis mode can be performed with less sample volume than normal mode (consult instruction manual for further information). However, automatic re-analysis cannot be performed.

5 Intended Use / Indications for Use

The Sysmex® CS-5100 is a fully automated blood coagulation analyzer intended for in vitro diagnostic use using plasma collected from venous blood samples in 3.2% sodium citrate tubes to analyze clotting, chromogenic and immunoassay methods in the clinical laboratory.

For determination of:

- Prothrombin Time (PT) seconds and PT INR with Dade® Innovin®
- Activated Partial Thromboplastin Time (APTT) with Dade® Actin® FSL
- Fibrinogen (Fbg) with Dade® Thrombin Reagent
- Coagulation Factor V with Dade® Innovin®
- Coagulation Factor VII with Dade® Innovin®
- Protein C with Protein C Reagent
- Antithrombin (AT) with INNOVANCE® Antithrombin
- Protein C with Berichrom® Protein C
- D-dimer with INNOVANCE® D-Dimer

The performance of this device has not been established in neonate and pediatric patient populations.

6 Comparison of Technological Characteristics with the Predicate Device

Both the subject and predicate instruments employ the same technological characteristics in that they automatically analyze various clotting tests using reagents, calibrators and controls previously cleared for automated coagulation analyzers. The reagents perform at least equally well on both the subject and predicate instruments. At a high level, the devices have the following same technological elements:

Similarities between CS-5100 and CA-1500

There are no technological differences between the subject and predicate devices. However the following minor changes exist between the subject and predicate devices:

Similarities between CS-5100 and CA-1500		
Analyzer Component	Proposed Device Sysmex® CS-5100	Predicate Device Sysmex® CA-1500
Regulatory Classification	JPA, Class II System, Multipurpose for in vitro coagulation studies	Same
Intended Use Statement	The Sysmex® CS-5100 is a fully automated blood coagulation analyzer intended for in vitro diagnostic use using plasma collected from venous blood samples in 3.2% sodium citrate tubes to analyze clotting, chromogenic and immunoassay methods in the clinical laboratory. For determination of: • Prothrombin Time (PT) seconds and PT INR with Dade® Innovin® • Activated Partial Thromboplastin Time (APTT) with Dade® Actin® FSL • Fibrinogen (Fbg) with Dade® Thrombin Reagent • Coagulation Factor V with Dade® Innovin® • Coagulation Factor VII with Dade® Innovin® • Protein C with Protein C Reagent • Antithrombin (AT) with INNOVANCE® Antithrombin • Protein C with Berichrom® Protein C • D-dimer with INNOVANCE® D-Dimer The performance of this device has not been established in neonate and pediatric patient populations.	The intended use of the Sysmex® CA-1500 is as a fully automated, computerized blood plasma coagulation analyzer for in vitro diagnostic use in clinical laboratories. The instrument uses citrated human plasma to perform the following parameters and calculated parameters: Clotting Analysis Parameters: Prothrombin Time (PT); Activated Partial Thromboplastin Time (APTT); Fibrinogen (Claus); Batroxobin Time; Extrinsic Factors (II, V, VII, X); Intrinsic Factors (VIII, IX, XI, XII); Protein C. Chromogenic Analysis Parameters: Antithrombin III; Factor VIII; Plasminogen; Heparin; Protein C; α2-Antiplasmin. Immunologic Analysis Parameters: D-dimer. Calculated Parameters: PT Ratio; PT INR; PT %; Derived Fibrinogen; Factor Assays % Activity.
Sample Type	Human plasma 3.2% sodium citrate	Same

Similarities between CS-5100 and CA-1500		
Analyzer Component	Proposed Device Sysmex® CS-5100	Predicate Device Sysmex® CA-1500
Application type	Clotting Applications: Prothrombin Time (PT) with Dade® Innovin®; Activated Partial Thromboplastin Time (APTT) with Dade® Actin® FSL; Fibrinogen (Clauss) with Dade® Thrombin Reagent; Coagulation Factor V with Dade® Innovin® Coagulation Factor VII with Dade® Innovin® Protein C with Protein C Reagent	Same
	Chromogenic Application: Antithrombin with INNOVANCE® Antithrombin; Protein C with Berichrom® Protein C	Same
	Immuno-Chemical Application: D-dimer with INNOVANCE® D-Dimer	Same
	Calculated Application: PT INR with Dade® Innovin®	Same
Specimen Processing	Automatic Pipetting and Dilution	Same
Random Access	Yes	Same
Liquid Level Sensing	Yes – reagent and sample	Same
Bar Code Reader	Sample + reagent	Same
STAT Testing	Yes	Same
Sampling Capabilities	Normal and Micro Mode	Same

Similarities between CS-5100 and CA-1500		
Analyzer Component	Proposed Device Sysmex® CS-5100	Predicate Device Sysmex® CA-1500
Sample Volumes (Plasma)	PT with Dade® Innovin® (50 µL) APTT with Dade® Actin® FSL (50 µL) Fibrinogen with Dade® Thrombin Reagent (10 µL) Coagulation Factor V with Dade® Innovin® (5 µL) Coagulation Factor VII with Dade® Innovin® (5 µL) Protein C with Protein C Reagent (5 µL) Protein C with Berichrom® Protein C (15 µL)	Same
Sample Volumes in Micro Mode (Plasma)	PT with Dade® Innovin® (50 µL) APTT with Dade® Actin® FSL (50 µL) Fibrinogen with Dade® Thrombin Reagent (10 µL) Coagulation Factor V with Dade® Innovin® (5 µL) Coagulation Factor VII with Dade® Innovin® (5 µL) Protein C with Protein C Reagent (5 µL) Protein C with Berichrom® Protein C (15 µL)	Same
Rinse & Buffer Solutions On-board External	CA-CLEAN I CA-CLEAN II Dade® Owren's Buffer Water	Same
Light Source Chromogenic Immuno-chemical	Halogen Lamp Halogen Lamp	Same Same

Similarities between CS-5100 and CA-1500		
Analyzer Component	Proposed Device Sysmex® CS-5100	Predicate Device Sysmex® CA-1500
Wavelengths* used in Analysis *The default wavelength is normally used to generate the reported value of the measurement. The sub-wavelength is run in parallel. If a light intensity error occurs by using the default wavelength the value from the sub-wavelength is used automatically.	Clotting Applications: Coagulation Factor V with Dade® Innovin® (Default = 660 nm; sub-wavelength = none) Coagulation Factor VII with Dade® Innovin® (Default = 660 nm; Sub-wavelength = none) Protein C with Protein C Reagent (Default = 660 nm; Sub-wavelength = none) Chromogenic Application: Antithrombin with INNOVANCE® Antithrombin (Default = 405 nm; Sub-wavelength = none) Protein C with Berichrom® Protein C (Default = 405 nm; Sub-wavelength = none)	Same
Temperature Control	Sample incubation well: 37 °C ± 1.0 °C	Same

Differences between CS-5100 and CA-1500

Differences between CS-5100 and CA-1500		
Analyzer Component	Proposed Device Sysmex® CS-5100	Predicate Device Sysmex® CA-1500
Operating Principle Clotting Chromogenic Immuno-Chemical	Transmitted Light Detection (Absorbance) at 340, 405, 575, 660 or 800 nm. Wavelengths 340 and 575 are technically available but not validated in combination with the intended applications. Transmitted Light Detection (Absorbance) at 340, 405, 575, 660, 800 nm. Wavelengths 340, 575, 660, and 800 are technically available but not validated in combination with the intended applications. Transmitted Light Detection (Absorbance) at 340, 405, 575, 660 or 800 nm. Wavelengths 340, 405, 575, and 800 are technically available but not validated in combination with the intended	Scattered Light Detection at 660 nm Transmitted Light Detection (Absorbance) at 405, 575, 800 nm Transmitted Light Detection (Absorbance) at 405, 575, or 800 nm
Wavelengths* used in Analysis *The default wavelength is normally used to generate the reported value of the measurement. The sub-wavelength is run in parallel. If a light intensity error occurs by using the default wavelength the value from the sub-wavelength is used automatically.	Clotting Applications: PT (seconds) with Dade® Innovin® (Default = 660 nm; Sub-Wavelength = 800 nm) PT (INR) with Dade® Innovin® (Default = 660 nm; Sub-Wavelength= 800 nm) APTT with Dade® Actin® FSL Activated PTT Reagent (Default = 660 nm; Sub-Wavelength= 800 nm) Fibrinogen with Dade® Thrombin Reagent (Default = 405 nm; Sub-Wavelength = none)	Clotting Applications: PT (seconds) with Dade® Innovin® (Default = 660 nm; Sub-Wavelength = none) PT (INR) with Dade® Innovin® (Default = 660 nm; Sub-Wavelength = none) APTT with Dade® Actin® FSL Activated PTT Reagent (Default = 660 nm; Sub-Wavelength= none) Fibrinogen with Dade® Thrombin Reagent (Default = 660 nm; Sub-Wavelength = none)

Differences between CS-5100 and CA-1500		
Analyzer Component	Proposed Device Sysmex® CS-5100	Predicate Device Sysmex® CA-1500
Wavelengths* used in Analysis *The default wavelength is normally used to generate the reported value of the measurement. The sub-wavelength is run in parallel. If a light intensity error occurs by using the default wavelength the value from the sub-wavelength is used automatically.	Immuno-chemical Application: D-dimer with INNOVANCE® D-Dimer (Default = 660 nm; Sub-Wavelength = none)	Immuno-chemical Application: D-dimer with INNOVANCE® D-Dimer (Default = 800 nm; Sub-Wavelength = none)
Light Source Clotting	Halogen Lamp	Light Emitting Diode
Probes	2 Sample probes; 3 Reagent probes	1 Sample probe; 1 Reagent probe
Cap Piercing	Cap Piercer only	Both options available: Cap Piercer and Non-Cap Piercer
Temperature Control	Detector: 37 ± 0.5 °C Reagent probe: 37.5 ± 0.5 °C	Detector: 37 ± 1.0 °C Reagent probe: 37 ± 1.0 °C
Reagent Cooling	10 ± 2 °C, when ambient temperature is 20 – 28 °C. During operation 4 – 15 °C, when ambient temperature is 15 – 30 °C	15 ± 2 °C, when ambient temperature is 15 – 30 °C
Pipetting Capabilities	Reagent probe: 20 – 200 µL Sample probe: 4 – 270 µL	Reagent probe: 3 – 200 µL Sample probe: 5 – 450 µL
Sample Volumes (Plasma)	Antithrombin with INNOVANCE® Antithrombin (14 µL) D-dimer with INNOVANCE® D-Dimer (15 µL)	Antithrombin with INNOVANCE® Antithrombin (10 µL) D-dimer with INNOVANCE® D-Dimer (13 µL)
Bidirectional Interface communication protocols	CA-, ASTM-, CS- Protocol	CA-, ASTM-Protocol

The above described differences do not raise new questions as to safety and effectiveness of the new device.

7 Performance Data

The following performance data were provided in support of the substantial equivalence determination.

7.1 Method comparison

Method comparison studies designed according to EP09-A3 CLSI Guideline ‘Measurement Procedure Comparison and Bias Estimation Using Patient Samples’ were conducted at four external sites in the United States, all sites using the same protocol.

Samples were measured on both the predicate device (Sysmex® CA-1500) as well as the new device (Sysmex® CS-5100), in random order to eliminate any inherent bias. Results were compared by Passing-Bablok regression analysis as well as Bland-Altman plots. Results from each application met the predetermined acceptance criteria. The following summary of Passing-Bablok regression shows that the proposed and predicate devices provide equivalent results when used in a clinical setting.

Sysmex® CS-5100: Method Comparison Summary Table, Passing-Bablok regression					
Application (measuring interval)	1st Site	2nd Site	3rd Site	4th Site	Sites Combined
Coagulation Factor V with Dade® Innovin® (6.0 - 149.0 % of norm)	N = 133 $y = 1.013 x - 0.205$ $r = 0.991$ ($r^2 = 0.983$)	N = 151 $y = 1.048 x - 1.431$ $r = 0.992$ ($r^2 = 0.983$)	N = 148 $y = 0.974 x + 0.853$ $r = 0.988$ ($r^2 = 0.975$)	N = 177 $y = 1.036 x + 1.319$ $r = 0.974$ ($r^2 = 0.950$)	N = 609 $y = 1.017 x + 0.185$ $r = 0.984$ ($r^2 = 0.969$)
Coagulation Factor VII with Dade® Innovin® (6.0 - 149.0 % of norm)	N = 121 $y = 1.040 x - 1.567$ $r = 0.993$ ($r^2 = 0.986$)	N = 145 $y = 1.017 x - 0.914$ $r = 0.993$ ($r^2 = 0.986$)	N = 102 $y = 1.081 x + 0.724$ $r = 0.995$ ($r^2 = 0.991$)	N = 137 $y = 1.117 x + 0.261$ $r = 0.987$ ($r^2 = 0.974$)	N = 505 $y = 1.051 x - 0.241$ $r = 0.989$ ($r^2 = 0.978$)
Protein C with Protein C Reagent (10.1 - 131.0 % of norm)	N = 138 $y = 1.005 x - 1.892$ $r = 0.996$ ($r^2 = 0.993$)	N = 176 $y = 1.006 x + 1.483$ $r = 0.994$ ($r^2 = 0.988$)	N = 110 $y = 0.891 x + 0.714$ $r = 0.993$ ($r^2 = 0.986$)	N = 200 $y = 0.973 x + 0.644$ $r = 0.984$ ($r^2 = 0.968$)	N = 624 $y = 0.988 x - 0.413$ $r = 0.987$ ($r^2 = 0.974$)
Protein C with Berichrom® Protein C (10.0 - 138.0 % of norm)	N = 127 $y = 0.963 x - 0.922$ $r = 0.995$ ($r^2 = 0.991$)	N = 149 $y = 0.935 x - 1.805$ $r = 0.992$ ($r^2 = 0.984$)	N = 130 $y = 0.923 x + 2.610$ $r = 0.995$ ($r^2 = 0.990$)	N = 125 $y = 0.985 x - 0.302$ $r = 0.994$ ($r^2 = 0.987$)	N = 531 $y = 0.950 x + 0.375$ $r = 0.992$ ($r^2 = 0.984$)

7.2 Reproducibility Studies

Twenty-day precision studies were performed at two external sites in Germany and one external site in the United States. Testing followed the scheme of two runs per day, with two replicates per run, at each of the three sites according to CLSI EP05-A2 'Evaluation of Precision Performance of Quantitative Measurement Methods'. The order of the analysis of parameter, samples and quality control samples for each run and day varied to avoid an inherent bias to the study. One calibration curve of each calibrated application was used in the study. Within Run, Between Run, Between Day, and Total (within site) were calculated. The data is summarized in the following tables.

Sysmex® CS-5100: Reproducibility Summary Table, Within Run				
Application (measuring interval)	1st Site <i>Within Run</i> (%CV)	2nd Site <i>Within Run</i> (%CV)	3rd Site <i>Within Run</i> (%CV)	Sites Combined (%CV)
Coagulation Factor V with Dade® Innovin® (6.0 - 149.0% of norm)	2.43 – 3.52	1.94 – 2.96	2.38 – 3.42	2.40 – 3.16
Coagulation Factor VII with Dade® Innovin® (6.0 - 149.0% of norm)	1.50 – 2.18	1.13 – 1.92	1.36 – 1.97	1.33 – 2.00
Protein C with Protein C Reagent (10.1 - 131.0% of norm)	3.00 – 3.83	2.11 – 2.94	1.80 – 2.47	2.53 – 3.22
Protein C with Berichrom® Protein C (10.0 - 138.0% of norm)	1.24 – 5.59	1.43 – 3.62	1.71 – 9.94	1.48 – 6.85

Sysmex® CS-5100: Reproducibility Summary Table, Between Run				
Application (measuring interval)	1 st Site Between Run (%CV)	2 nd Site Between Run (%CV)	3 rd Site Between Run (%CV)	Sites Combined (%CV)
Coagulation Factor V with Dade® Innovin® (6.0 - 149.0% of norm)	4.08 – 5.33	2.22 – 3.72	2.55 – 4.21	3.29 – 4.24
Coagulation Factor VII with Dade® Innovin® (6.0 - 149.0% of norm)	0.39 – 1.80	0.00 – 0.93	0.64 – 1.09	0.65 – 1.29
Protein C with Protein C Reagent (10.1 - 131.0% of norm)	2.51 – 3.96	0.00 – 1.68	1.48 – 5.51	1.73 – 3.86
Protein C with Berichrom® Protein C (10.0 - 138.0% of norm)	0.00 – 2.56	0.00 – 1.44	0.00 – 1.14	0.00 – 1.04

Sysmex® CS-5100: Reproducibility Summary Table, Between Day				
Application (measuring interval)	1 st Site Between Day (%CV)	2 nd Site Between Day (%CV)	3 rd Site Between Day (%CV)	Sites Combined (%CV)
Coagulation Factor V with Dade® Innovin® (6.0 - 149.0% of norm)	0.00 – 0.00	0.88 – 2.61	0.00 – 2.72	0.00 – 0.59
Coagulation Factor VII with Dade® Innovin® (6.0 - 149.0% of norm)	0.00 – 1.64	1.49 – 2.66	0.95 – 2.05	0.94 – 1.97
Protein C with Protein C Reagent (10.1 - 131.0% of norm)	0.00 – 1.57	0.00 – 2.31	0.00 – 0.52	0.00 – 1.01
Protein C with Berichrom® Protein C (10.0 - 138.0% of norm)	0.00 – 1.33	0.00 – 0.90	0.46 – 2.75	0.39 – 1.16

CS-5100: Reproducibility Summary Table, Total CV (Within Site and Sites Combined)				
Application (measuring interval)	1st Site Total CV Within Site (%CV)	2nd Site Total CV Within Site (%CV)	3rd Site Total CV Within Site (%CV)	Total CV Sites Combined (%CV)
Coagulation Factor V with Dade® Innovin® (6.0 - 149.0% of norm)	4.85 – 6.06	3.75 – 5.06	3.54 – 5.30	4.83 – 6.85
Coagulation Factor VII with Dade® Innovin® (6.0 - 149.0% of norm)	1.87 – 2.82	1.83 – 2.96	2.15 – 2.87	3.39 – 5.03
Protein C with Protein C Reagent (10.1 - 131.0% of norm)	4.25 – 5.51	2.45 – 4.10	2.49 – 6.04	4.54 – 7.15
Protein C with Berichrom® Protein C (10.0 - 138.0% of norm)	1.34 – 6.15	1.65 – 3.88	2.27 – 9.95	3.22 – 7.92

7.3 Detection Capability Results

Detection capability studies were measured for the calibrated assays on the Sysmex® CS-5100: Coagulation Factor V with Dade® Innovin®, Coagulation Factor VII with Dade® Innovin®, Protein C with Protein C Reagent, and Protein C with Berichrom® Protein C. Studies were conducted following the CLSI document EP17-A2 'Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures'. Data for all tested reagents met the predetermined acceptance criteria and support the lower limit of the clinically reportable range claim.

Sysmex® CS-5100: Summary of Limit of Quantitation Studies			
Application	Lower Limit of Clinically Reportable Range (% of norm)	Measured Limit of Quantitation based on predicate device (% of norm)	Maximum Total Error (% of norm)
Coagulation Factor V with Dade® Innovin®	6.0	4.80	0.74
Coagulation Factor VII with Dade® Innovin®	6.0	3.39	0.27
Protein C with Protein C Reagent	10.1	9.35	2.91
Protein C with Berichrom® Protein C	10.0	8.32	2.07

7.4 Linearity & Measuring Range

Linearity studies were performed for the calibrated assays on the Sysmex® CS-5100: Coagulation Factor V with Dade® Innovin®, Coagulation Factor VII with Dade® Innovin®, Protein C with Protein C Reagent, and Protein C with Berichrom® Protein C. All reagents met the predetermined acceptance criteria and support the clinically reportable range claim. Studies were conducted as described in CLSI EP6-A 'Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach'.

Sysmex® CS-5100: Linearity and Measuring Range Summary		
Application	Measured Linear Range	Clinically Reportable Range
Coagulation Factor V with Dade® Innovin®	3.4 – 180.7% of norm	6.0 – 149.0% of norm
Coagulation Factor VII with Dade® Innovin®	4.3 – 179.5% of norm	6.0 – 149.0% of norm
Protein C with Protein C Reagent	7.0 – 187.7% of norm	10.1 – 131.0% of norm
Protein C with Berichrom® Protein C	7.1 – 181.3% of norm	10.0 – 138.0% of norm

7.5 Reference Interval

Reference interval studies were conducted at three clinical study sites in the United States following the guidance of CLSI document EP28-A3c '*Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory*'. The summary is provided below. The study population did not include neonate and pediatric sample populations.

Sysmex® CS-5100: Reference Interval Summary Table		
Application	N	Sysmex® CS-5100 Reference Interval
Coagulation Factor V with Dade® Innovin®	194	80.8% of norm (5 th Percentile)
Coagulation Factor VII with Dade® Innovin®	194	67.6% of norm (5 th Percentile)
Protein C with Protein C Reagent	194	76.4% of norm (5 th Percentile)
Protein C with Berichrom® Protein C	194	83.0% of norm (5 th Percentile)

8 Conclusions

Because the predicate device was cleared based in part on the results of clinical studies, and because clinical settings are required for a well-validated device, clinical testing was required to support substantial equivalence.

The non-clinical data support the safety of the device.

The clinical data demonstrate that the Sysmex® CS-5100 performs comparably to the predicate device that is currently marketed for the same intended use.

The data submitted for this premarket notification demonstrates that the device raises no new concerns as to safety and effectiveness when compared to the predicate device, and is substantially equivalent to the predicate device.