October 31, 2017

Siemens Healthcare Diagnostics Products GmbH
Donna Noeh
Regulatory Affairs Manager
Emil-von-Behring Strasse 76
Marburg, Hessen 35041 Germany

Re: K172333
Trade/Device Name: Sysmex® Automated Blood Coagulation Analyzer CS-5100
Regulation Number: 21 CFR 864.5425
Regulation Name: Multipurpose system for in vitro coagulation studies
Regulatory Class: Class II
Product Code: JPA, GGW, GJT, GIR
Dated: July 21, 2017
Received: August 2, 2017

Dear Donna Noeh:

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 Part 801 and Part 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 and Part 809), please contact the Division of Industry and Consumer Education (DICE) 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 (DICE) 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

Lea Carrington
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K172333

Device Name
Sysmex® Automated Blood Coagulation Analyzer CS-5100, Factor V Leiden Assay, Coagulation Factor VIII, IX, XI and XII Deficient Plasmas, LA1 Screening and LA2 Confirmation Reagents

Indications for Use *(Describe)*
The Sysmex® Automated Blood Coagulation Analyzer 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®
- Coagulation Factor VIII with Dade® Actin® FSL
- Coagulation Factor IX with Dade® Actin® FSL
- Lupus Anticoagulant with LA1 Screening and LA2 Confirmation Reagent
- Factor V Leiden with Factor V Leiden Assay
- 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.

Intended Use for Factor V Leiden Assay:
The Siemens Healthcare Diagnostics Factor V Leiden Assay is a simple functional clotting test system intended for screening of resistance to Activated Protein C (APC) in plasma from individuals with Factor V (Leiden) defect. For in vitro diagnostic use.

Intended Use for Coagulation Factor VIII Deficient Plasma:
In vitro diagnostic reagents for the determination of the activity of coagulation factors VIII, IX, XI and XII in human plasma by coagulation methods.

Intended Use for Coagulation Factor IX Deficient Plasma:
In vitro diagnostic reagents for the determination of the activity of coagulation factor VIII, IX, XI and XII in human plasma by coagulation methods.

Intended Use for LA1 Screening and LA2 Confirmation Reagents:
LA1 Screening Reagent and LA2 Confirmation Reagent are simplified DRVVT reagents for detection of Lupus Anticoagulants (LA) in one-stage clotting tests. LA1 Screening Reagent: Simplified DRVV reagent to screen for the presence of Lupus Anticoagulants. LA2 Confirmation Reagent: Phospholipid-rich DRVV reagent for the specific correction of Lupus Anticoagulants.

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:	October 19, 2017

2 Device

Name of Device:	Sysmex® Automated Blood Coagulation Analyzer CS-5100
Common or Usual Name:	Automated Coagulation Instrument
Classification Name:	Multipurpose system for in vitro coagulation studies (21 CFR 864.5425)
Regulatory Class:	2
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:	2
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
Factor V Leiden Assay *The Siemens Healthcare Diagnostics Factor V Leiden Assay is a simple functional clotting test system intended for screening of resistance to Activated Protein C (APC) in plasma from individuals with the Factor V (Leiden) defect. For in vitro diagnostic use.*	K992456	864.7925	Class II	GGW	Hematology
Coagulation Factor VIII Deficient Plasma *In vitro diagnostic reagents for the determination of the activity of coagulation factors VIII, IX, XI and XII in human plasma by coagulometric methods.*	K924396	864.7290	Class II	GJT	Hematology
Coagulation Factor IX Deficient Plasma *In vitro diagnostic reagents for the determination of the activity of coagulation factors VIII, IX, XI and XII in human plasma by coagulometric methods.*	K924396	864.7290	Class II	GJT	Hematology
LA 1 Screening Reagent, LA 2 Confirmation Reagent, and LA Ratio *LA 1 Screening Reagent and LA 2 Confirmation Reagent are simplified DRVVT reagents for detection of Lupus Anticoagulants (LA) in one-stage clotting tests. LA 1 Screening Reagent: Simplified DRVV reagent to screen for the presence of Lupus Anticoagulants. LA 2 Confirmation Reagent: Phospholipid-rich DRVV reagent for the specific correction of Lupus Anticoagulants.*	K993299	864.8950	Class I	GIR	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 Factor V Leiden with Factor V Leiden Assay, Coagulation Factor VIII with Dade® Actin FSL®, Coagulation Factor IX with Dade® Actin FSL®, Lupus Anticoagulant with LA 1 Screening Reagent and LA 2 Confirmation Reagent.

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.

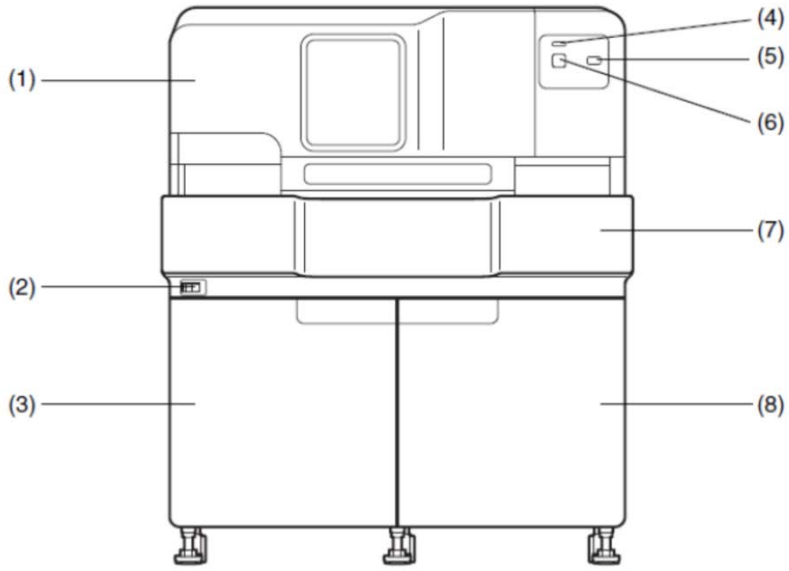
Table of Sysmex® CS-5100 Analysis Principles

Reagent	Application	Methodology
Factor V Leiden Assay	Factor V Leiden with Factor V Leiden Assay	Clotting (extrinsic pathway); Calculated
Coagulation Factor VIII Deficient Plasma	Coagulation Factor VIII with Dade® Actin FSL®	Clotting (intrinsic pathway)
Coagulation Factor IX Deficient Plasma	Coagulation Factor IX with Dade® Actin FSL®	Clotting (intrinsic pathway)
LA 1 Screening Reagent	Lupus Anticoagulant with LA 1 Screening Reagent	Clotting
LA 2 Confirmation Reagent	Lupus Anticoagulant with LA 2 Confirmation Reagent	Clotting
LA 1 Screening Reagent and LA 2 Confirmation Reagent	LA Ratio with LA 1 Screening Reagent and LA 2 Confirmation Reagent	Clotting; Calculated

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

Instrument (main unit)

Figure 1: Front View of the Sysmex CS-5100 (main unit)



(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.

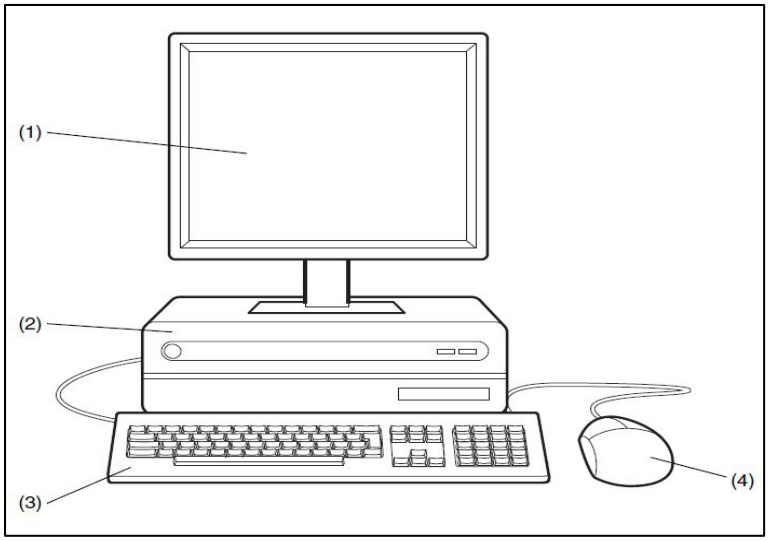
(5) Mechanical stop switch: Press this switch to immediately stop the instrument's mechanical movement.

(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.

Figure 2: Informational Processing Unit (IPU) Sysmex CS-5100



(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.

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. Automatic re-analysis can also be performed.

(2) Micro-sample mode: The sample volume from samples set in the sampler or STAT holder is taken into the instrument for each analysis through dispensing sample probe and analyzed. This analysis mode can also be performed with less sample volume than normal mode; however, automatic re-analysis cannot be performed.

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.

5 Similarities between Sysmex CS-5100 and Sysmex CA-1500

Similarities between Sysmex CS-5100 and Sysmex CA-1500		
Analyzer Component	**Proposed Device Sysmex® CS-5100**	**Predicate Device Sysmex® CA-1500**
Regulatory Classification	JPA, Class 2 System, Multipurpose for in vitro coagulation studies	Same
Intended 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® • Coagulation Factor VIII with Dade® Actin® FSL • Coagulation Factor IX with Dade® Actin® FSL • Lupus Anticoagulant with LA1 Screening and LA2 Confirmation Reagent • Factor V Leiden with Factor V Leiden Assay • 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 (Clauss); 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.

Similarities between Sysmex CS-5100 and Sysmex CA-1500		
Analyzer Component	**Proposed Device Sysmex® CS-5100**	**Predicate Device Sysmex® CA-1500**
Sample Type	Human plasma 3.2% sodium citrate	Same
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® Coagulation Factor VIII with Dade® Actin® FSL Coagulation Factor IX with Dade® Actin® FSL Lupus Anticoagulant with LA 1 Screening and LA 2 Confirmation Reagents Factor V Leiden with Factor V Leiden Assay 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

Similarities between Sysmex CS-5100 and Sysmex CA-1500		
Analyzer Component	**Proposed Device Sysmex® CS-5100**	**Predicate Device Sysmex® CA-1500**
Clinical Reportable Range	Coagulation Factor VIII with Dade® Actin® FSL: 3.0 – 182.0.0% of norm; Coagulation Factor IX with Dade® Actin® FSL: 3.0 – 145.5%; Factor V Leiden with Factor V Leiden Assay: 0.72 – 5.91 ratio; LA 1 with LA 1 Screening Reagent: 24.9 – 158.8 sec.	Same
Specimen Processing	Automatic Pipetting and Dilution	Same
Random Access	Yes	Same
Liquid Level Sensing	Yes – reagent and sample	Same
Bar Code Reader	Sample and reagent	Same
STAT Testing	Yes	Same
Sampling Capabilities	Normal and Micro Mode	Same

Similarities between Sysmex CS-5100 and Sysmex 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) Coagulation Factor VIII with Dade® Actin FSL® (2 µL) Coagulation Factor IX with Dade® Actin FSL® (2 µL) Lupus Anticoagulant with LA1 Screening Reagent (100 µL) Lupus Anticoagulant with LA2 Confirmation Reagent (100 µL) Factor V Leiden with Factor V Leiden Assay (50 µL)	Same

Similarities between Sysmex CS-5100 and Sysmex CA-1500		
Analyzer Component	**Proposed Device Sysmex® CS-5100**	**Predicate Device Sysmex® CA-1500**
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) Coagulation Factor VIII with Dade® Actin FSL® (2 µL) Coagulation Factor IX with Dade® Actin FSL® (2 µL) Lupus Anticoagulant with LA1 Screening Reagent (100 µL) Lupus Anticoagulant with LA2 Confirmation Reagent (100 µL) Factor V Leiden with Factor V Leiden Assay (50 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 Light emitted diode
Probes	1 Sample probe; 1 Reagent probe	Same

Similarities between Sysmex CS-5100 and Sysmex CA-1500		
Analyzer Component	**Proposed Device Sysmex® CS-5100**	**Predicate Device Sysmex® CA-1500**
Wavelengths used in Analysis	Coagulation Factor VIII with Dade® Actin FSL® (Default = 660 nm; Sub-wavelength= none) Coagulation Factor IX with Dade® Actin FSL® (Default = 660 nm; Sub-wavelength= none) Lupus Anticoagulant with LA1 Screening Reagent (Default = 660 nm; Sub-wavelength=none) Lupus Anticoagulant with LA2 Confirmation Reagent (Default = 660 nm; Sub-wavelength=none) Factor V Leiden with Factor V Leiden Assay (Default = 660 nm; Sub-wavelength= none)	Same
Temperature Control	Sample incubation well: 37 °C ± 1.0 °C	Same

6. Differences between Sysmex CS-5100 and CA-1500

Differences between Sysmex CS-5100 and Sysmex CA-1500		
Analyzer Component	**Proposed Device Sysmex® CS-5100**	**Predicate Device Sysmex® CA-1500**
Operating Principle	Clotting: Transmitted Light Detection (Absorbance) at 340, 405, 575, 660 or 800 nm. Wavelengths 340, 405 and 575 are technically available but not validated in combination with the intended applications. Chromogenic: 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. Immunochemical: 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 applications.	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
Light Source Clotting	Halogen Lamp	Light Emitting Diode
Cap Piercing	Cap Piercer only	Both Cap Piercer model and Non-Cap Piercer models are available
Temperature Control	Detector: 37 ± 0.5 ºC Reagent probe: 37.5 ± 0.5 ºC	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: 4 – 200 µL Sample probe: 5 – 450 µL

Differences between Sysmex CS-5100 and Sysmex CA-1500		
Analyzer Component	**Proposed Device Sysmex® CS-5100**	**Predicate Device Sysmex® CA-1500**
Clinical Reportable Range	LA2 with LA 2 Confirmation Reagent: 32.2 – 80.0 sec.; LA Ratio with LA 1 / LA 2 reagent : 0.71 – 2.60 ratio	LA2 with LA 2 Confirmation Reagent: 32.2 – 111.2 sec.; LA Ratio with LA 1 / LA 2 reagent : 0.71 – 2.98 ratio
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)
Probes	2 Sample probes; 3 Reagent probes	1 Sample probe; 1 Reagent probe

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; 3 in the United States and one in Germany, 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	1st Site	2nd Site	3rd Site	4th Site	Sites Combined
Factor V Leiden with Factor V Leiden Assay (Ratio)	N = 87 y = 0.965 x + 0.137 r = 0.991 (r^2 = 0.983)	N = 173 y = 0.958 x + 0.052 r = 0.996 (r^2 = 0.991)	N = 84 y = 1.039 x + 0.040 r = 0.979 (r^2 = 0.959)	N = 151 y = 1.010 x + 0.005 r = 0.946 (r^2 = 0.895)	N = 495 y = 0.976 x + 0.058 r = 0.983 (r^2 = 0.967)
Coagulation Factor VIII with Dade® Actin® FSL (% of norm)	N = 83 y = 1.128 x – 7.297 r = 0.954 (r^2 = 0.910)	N = 155 y = 1.010 x - 1.157 r = 0.992 (r^2 = 0.985)	N = 72 y = 1.010 x + 3.199 r = 0.951 (r^2 = 0.904)	N = 122 y = 1.046 x – 1.651 r = 0.920 (r^2 = 0.847)	**N = 432** **y = 1.054 x – 2.558** **r = 0.966** **(r^2 = 0.933)**
Coagulation Factor IX with Dade® Actin® FSL (% of norm)	N = 87 y = 1.021 x – 1.607 r = 0.982 (r^2 = 0.964)	N = 146 y = 1.011 x – 0.763 r = 0.991 (r^2 = 0.982)	N = 73 y = 0.999 x + 1.627 r = 0.972 (r^2 = 0.944)	N = 169 y = 1.003 x – 1.474 r = 0.985 (r^2 = 0.971)	**N = 475** **y = 1.014 x – 1.227** **r = 0.985** **(r^2 = 0.970)**
Lupus Anticoagulant with LA 1 Screening Reagent (seconds)	N = 4 y = n/a r = n/a (r^2 = n/a)	N = 112 y = 0.941 x + 3.738 r = 0.997 (r^2 = 0.993)	N = 88 y = 0.965 x + 0.470 r = 0.993 (r^2 = 0.986)	N = 165 y = 0.902 x + 3.043 r = 0.994 (r^2 = 0.987)	**N = 369** **y = 0.952 x + 1.523** **r = 0.993** **(r^2 = 0.986)**

Sysmex® CS-5100: Method Comparison Summary Table, Passing-Bablok regression					
Application	**1st Site**	**2nd Site**	**3rd Site**	**4th Site**	**Sites Combined**
Lupus Anticoagulant with LA 2 Confirmation Reagent (seconds)	N = 17 y = n/a r = n/a (r^2 = n/a)	N = 118 y = 0.972 x + 2.254 r = 0.996 (r^2 = 0.992)	N = 79 y = 0.938 x + 2.369 r = 0.997 (r^2 = 0.994)	N = 139 y = 0.928 x + 1.999 r = 0.989 (r^2 = 0.979)	**N = 353** **y = 0.964 x + 1.219** **r = 0.989** **(r^2 = 0.978)**
Lupus Anticoagulant with LA1/ LA2 Ratio (Ratio)	N = 4 y = n/a r = n/a (r^2 = n/a)	N = 106 y = 0.933 x + 0.071 r = 0.990 (r^2 = 0.979)	N = 71 y = 0.992 x – 0.012 r = 0.988 (r^2 = 0.976)	N = 125 y = 0.917 x + 0.078 r = 0.992 (r^2 = 0.984)	**N = 306** **y = 0.942 x + 0.054** **r = 0.990** **(r^2 = 0.980)**

7.2 Reproducibility Studies

Twenty-day precision studies were performed at one external site in Germany and two external sites 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 for Within Run and Total (within site) is summarized in the following tables.

Sysmex® CS-5100: Reproducibility Summary Table, Within Run				
Application	**1st Site *Within Run* (%CV)**	**2nd Site *Within Run* (%CV)**	**3rd Site *Within Run* (%CV)**	**Sites Combined (%CV)**
Factor V Leiden with Factor V Leiden Assay	0.82 – 4.82	0.70 – 1.39	0.58 – 1.98	0.82 – 3.08
Coagulation Factor VIII with Dade® Actin® FSL	2.29 – 3.95	1.94 -4.20	2.04 – 5.25	2.15 – 4.46
Coagulation Factor IX with Dade® Actin® FSL	1.79 – 4.70	2.01 – 4.11	2.26 – 4.63	2.12 – 4.49
Lupus Anticoagulant with LA 1 Screening Reagent (seconds)	0.58 – 3.29	0.51 – 2.52	0.51 – 2.33	0.60 – 2.75
Lupus Anticoagulant with LA 2 Confirmation Reagent (seconds)	0.55 – 2.58	0.26 – 1.36	0.32 – 1.52	0.27 – 1.18
Lupus Anticoagulant with LA1/ LA2 Ratio (Ratio)	0.51 -1.38	0.61 – 1.04	0.58 – 1.47	0.59 – 1.14

Sysmex® CS-5100: Reproducibility Summary Table, Total CV (Within Site and Sites Combined)				
Application	**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)**
Factor V Leiden with Factor V Leiden Assay	1.10 – 5.25	1.00 – 3.96	0.90 – 2.62	2.15 – 5.91
Coagulation Factor VIII with Dade® Actin® FSL	4.45 – 6.30	2.88 – 4.80	3.78 – 6.09	4.02 – 7.12
Coagulation Factor IX with Dade® Actin® FSL	4.58 – 9.13	2.25 – 5.12	3.96 – 6.71	4.34 – 7.26
Lupus Anticoagulant with LA 1 Screening Reagent (seconds)	0.80 – 3.90	1.09 – 2.83	1.39 – 3.29	1.38 – 3.34
Lupus Anticoagulant with LA 2 Confirmation Reagent (seconds)	0.41 – 1.42	0.55 – 1.54	0.51 – 1.45	0.90 – 1.91
Lupus Anticoagulant with LA1/ LA2 Ratio (Ratio)	0.93 – 2.26	0.96 – 3.45	0.96 – 2.78	1.16 – 3.45

7.3 Detection Capability Results

Detection capability studies were measured for the calibrated assays on the Sysmex® CS-5100: Coagulation Factor VIII with Dade® Actin® FSL and Coagulation Factor IX with Dade® Actin® FSL. 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 VIII with Dade® Actin® FSL	3.0	2.52	0.50
Coagulation Factor IX with Dade® Actin® FSL	3.0	2.76	1.07

7.4 Linearity & Measuring Range

Linearity studies were performed for the calibrated assays on the Sysmex® CS-5100: Coagulation Factor VIII with Dade® Actin® FSL and Coagulation Factor IX with Dade® Actin® FSL. 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 (% of Norm)**	**Clinically Reportable Range (% of Norm)**
Coagulation Factor VIII with Dade® Actin® FSL	2.12 – 246.41	3.0 – 182.0
Coagulation Factor IX with Dade® Actin® FSL	2.38 – 193.79	3.0 – 145.5

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**
Factor V Leiden with Factor V Leiden Assay	193	1.47 Ratio (2.5th Percentile)
Coagulation Factor VIII with Dade® Actin® FSL	190	82.0% of norm (2.5th Percentile)
Coagulation Factor IX with Dade® Actin® FSL	188	81.4% of norm (2.5th Percentile)
Lupus Anticoagulant with LA 1 Screening Reagent (fresh samples)	185	32.2 seconds (2.5th Percentile)
Lupus Anticoagulant with LA 1 Screening Reagent (frozen samples)	191	32.8 seconds (2.5th Percentile)
Lupus Anticoagulant with LA 2 Confirmation Reagent (fresh samples)	185	34.7 seconds (2.5th Percentile)
Lupus Anticoagulant with LA 2 Confirmation Reagent (frozen samples)	191	35.7 seconds (2.5th Percentile)
Lupus Anticoagulant with LA1/ LA2 Ratio (fresh samples)	184	0.89Ratio (2.5th Percentile)
Lupus Anticoagulant with LA1/ LA2 Ratio (frozen samples)	191	0.91 Ratio (2.5th Percentile)

7.6 Factor V Leiden Cut-off Study

A cut-off of 1.8 (ratio) was validated on the CS-5100 instrument in a performance evaluation study. Citrated plasma samples from patients submitted for thrombophilia screening were collected by three different clinical sites (one site in the US and two sites in Germany). The samples were frozen and measured with the FV Leiden assay on the CS-5100 instrument. The FV Leiden assay results were classified using the cut-off of 1.8: a ratio ≤1.8 is suggestive for FV Leiden variant (single point mutation G1691A) and a ratio >1.8 is considered as negative for the FV Leiden variant. The FV Leiden assay results were subsequently compared to the Factor V Leiden genotype to calculate the positive and negative percentage agreement. In total, n=381 patients of which n=127 patients came from the US were included. The results are shown in the tables below.

All sites combined (US and OUS)		Reference (Factor V Leiden PCR method)		
		Negative	Positive	Total
Factor V Leiden assay on Sysmex® CS-5100 System	Negative	161	0	161
	Positive	0	220	220
	Total	161	220	381

Sensitivity =	100.0%	95.0% Confidence Interval =	98.3 – 100.0%
Specificity =	100.0%	95.0% Confidence Interval =	97.7 – 100.0%

8 Conclusion

The predicate device was cleared based in part on the results of clinical studies; therefore clinical testing was required to support substantial equivalence.

The non-clinical and 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.