DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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September 01, 2016

Siemens Healthcare Diagnostics Products GmbH
Mr. Nils Neumann
Regulatory Manager, US Affairs
Emil-von-Behring-Str. 76
35041 Marburg, Germany

Re: K161312
Trade/Device Name: Sysmex CS-2100i
Regulation Number: 21 CFR 864.5425
Regulation Name: Multipurpose system for in vitro coagulation studies
Regulatory Class: Class II
Product Code: JPA
Dated: July 28, 2016
Received: August 1, 2016

Dear Mr. Neumann:

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" (21CFR 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 yours,

Kelly Oliner -S

For,
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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement on last page.

510(k) Number *(if known)*
K161312

Device Name
Sysmex CS-2100i

Indications for Use *(Describe)*
The Sysmex CS-2100i 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
• Antithrombin (AT) with INNOVANCE® Antithrombin
• D-dimer with INNOVANCE® D-Dimer.
The performance of this device has not been established in neonate and pediatric patient populations.

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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

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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 26, 2016

2. Device

Name of Device:	Sysmex CS-2100i
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.

4. Device Description / Test Principle

The Sysmex CS-2100i 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 is to expand the use of the INNOVANCE® D-Dimer for the exclusion of Deep Vein Thrombosis on Sysmex CS-2100i. All other established indications, performance and technology characteristics as cleared under K151259 remain unchanged.

5. Intended Use / Indications for Use

The Sysmex CS-2100i 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
- Antithrombin (AT) with INNOVANCE® Antithrombin
- 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:

Device Comparison Table

Similarities to the Predicate Device

Similarities between Sysmex CS-2100i and Sysmex CA®-1500		
Analyzer Component	**Proposed Device** Sysmex CS-2100i	**Predicate Device** Sysmex CA®-1500
Regulatory Classification	JPA Class 2 System, Multipurpose for in vitro coagulation studies	Same
Intended Use Statement	The Sysmex CS-2100i 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 • Antithrombin (AT) with INNOVANCE® Antithrombin •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 Prameters: 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

Similarities between Sysmex CS-2100i and Sysmex CA®-1500		
Analyzer Component	**Proposed Device** Sysmex CS-2100i	**Predicate Device** Sysmex CA®-1500
		Parameters: D-dimer. Calculated Parameters: PT Ratio; PT INR; PT %; Derived Fibrinogen; Factor Assays % Activity
Application	Immuno-chemical Application: D-dimer with INNOVANCE® D-Dimer	Same
Sample Type	Human plasma, 3.2% sodium citrate	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
Sample Volumes in Normal Mode	D-dimer with INNOVANCE® D-Dimer 13 µL	Same

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

Differences between Sysmex CS-2100i and Sysmex CA®-1500		
Analyzer Component	**Proposed Device** Sysmex CS-2100i	**Predicate Device** Sysmex CA®-1500
Operating Principle Immuno-chemical	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.	Optical Density 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.	D-dimer with INNOVANCE® D-Dimer (Default = 660 nm; Sub-Wavelength= none)	D-dimer with INNOVANCE® D-Dimer (Default = 800 nm; Sub-Wavelength= none)
Light Source Clotting	Halogen Lamp	Light Emitting Diode
Cap Piercing	Cap Piercer only	Both options available: Cap Piercer and No-Cap Piercer
Temperature Control	-Detector : 37 ºC ± 0.5 ºC -Reagent incubation probe : 37.5 ºC ± 0.5 ºC	-Detector: 37°C ± 1.0°C -Reagent incubation probe: 37°C ± 1.0°C

Differences between Sysmex CS-2100i and Sysmex CA®-1500		
Analyzer Component	**Proposed Device** Sysmex CS-2100i	**Predicate Device** Sysmex CA®-1500
Reagent Cooling	10°C ± 2°C, when ambient temperature is 20°C – 28°C. During operation 4°C -15°C, when ambient temperature is 15°C – 30°C	15°C ± 2°C, when ambient temperature is 15°C – 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 in Micro Mode (Plasma)	15 µL	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

Performance Data: Extended indication for the exclusion of deep vein thrombosis (DVT). See original submission (K151259) for previously conducted analytical and clinical studies:

- Method comparison
- Reproducibility
- Detection Capability
- Linearity & Measuring Range
- Reference Interval
- D-dimer PE exclusion validation

7.1 D-Dimer DVT Exclusion Validation Study

The INNOVANCE® D-Dimer assay was evaluated on the Sysmex CS-2100i System in a multi-center study to validate the exclusion of a first event of Deep Vein Thrombosis (DVT) using frozen specimens collected prospectively from 1907 consecutive outpatients presenting to the emergency or ambulatory department with suspected DVT. Of these 1907 patients, 368 were excluded from analysis (including 213 patients reported to have a previously documented or chronic DVT) resulting in a total of 1539 patients. All potentially eligible patients were evaluated using the Wells' rules to estimate their pre-test probability (PTP) with regard to DVT, and then categorized into likely or unlikely, or alternatively as high, intermediate or low PTP. Patients with a high PTP score were excluded from enrollment. Patients with no or a positive D-dimer result with the D-dimer assay used at the respective study center were evaluated by imaging methods, e.g. ultrasound. Patients with a negative D-dimer result with the D-dimer assay used at the respective study center underwent imaging at the physician's discretion. All patients with a negative clinical diagnosis of DVT at presentation were followed up after three months to evaluate potential development of DVT. Patients with unobtainable follow-up data were excluded from analysis resulting in n= 1317 patients available for final analysis. The overall prevalence of DVT in the 1317 patients was 6.1 % (80 of 1317) with 7.0 % in the US population and 4.7 % in the European population.

The specimens were tested with the INNOVANCE® D-Dimer assay and results were compared to a cut-off value of 0.50 mg/L FEU. A D-dimer result <0.50 mg/L FEU was considered negative and a D-dimer result ≥0.50 mg/L FEU was considered positive. The instrument-specific sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) with lower bound (LCL) of a two-sided 95 % confidence interval were calculated. Results obtained for each study population are detailed below.

US sites DVT		Reference (Imaging and 3-month follow-up)		
		Positive	Negative	Total
INNOVANCE® D-Dimer on CS-2100i	Positive	55	450	505
	Negative	1	297	298
	Total	56	747	803

Sensitivity %=	98.2	95% LCL=	90.4
Specificity %=	39.8	95% LCL=	36.2
NPV %=	99.7	95% LCL=	98.1
NPV* %=	99.2	95% LCL=	95.7
PPV %=	10.9	95% LCL=	8.5
PPV* %=	22.3	95% LCL=	17.9

*standardized to a prevalence of 15%

OUS sites DVT		Reference (Imaging and 3-month follow-up)		
		Positive	Negative	Total
INNOVANCE® D-Dimer on CS-2100i	Positive	23	217	240
	Negative	1	273	274
	Total	24	490	514

Sensitivity %=	95.8	95% LCL=	78.9
Specificity %=	55.7	95% LCL=	51.2
NPV %=	99.6	95% LCL=	98.0
NPV* %=	98.7	95% LCL=	93.0
PPV %=	9.6	95% LCL=	6.5
PPV* %=	27.6	95% LCL=	20.0

*standardized to a prevalence of 15%

US and OUS sites DVT		Reference (Imaging and 3-month follow-up)		
		Positive	Negative	Total
NNOVANCE® D-Dimer on CS-2100i	Positive	78	667	745
	Negative	2	570	572
	Total	80	1237	1317

Sensitivity %=	97.5	95% LCL=	91.3
Specificity %=	46.1	95% LCL=	43.3
NPV %=	99.7	95% LCL=	98.7
NPV* %=	99.1	95% LCL=	96.6
PPV %=	10.5	95% LCL=	8.5
PPV* %=	24.2	95% LCL=	20.2

*standardized to a prevalence of 15%

Note:
For the exclusion of deep vein thrombosis (DVT) the diagnostic performance was assessed in a population of patients with the suspicion of a first event of DVT. For other patient populations (e. g. with recurrent or chronic DVT) the effectiveness of the device to exclude DVT has not been verified.

8. Conclusion

The modified Sysmex CS-2100i Coagulation Analyzer, with the expanded indication of the INNOVANCE® D-Dimer for the exclusion of Deep Vein Thrombosis, is substantially equivalent to the legally marketed predicate device FDA cleared under K011235.