

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY**

**A. 510(k) Number:**

K161312

**B. Purpose for Submission:**

The purpose of this submission is to extend the use of the previously cleared INNOVANCE® D-dimer assay (K093626) for the exclusion of deep vein thrombosis (DVT) to the Sysmex CS-2100i.

In addition to the INNOVANCE® D-dimer assay for the exclusion of pulmonary embolism (PE), the Sysmex CS-2100i was also cleared for the following assays: 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, and Antithrombin (AT) with INNOVANCE® Antithrombin in the premarket notification K151259.

**C. Manufacturer and Instrument Name:**

Sysmex Corporation; Sysmex CS-2100i

**D. Type of Test or Tests Performed:**

Quantitative coagulation test: INNOVANCE® D-Dimer with the following intended use:

For the quantitative determination of cross-linked fibrin degradation products (D-dimers) in human plasma on Siemens Healthcare Diagnostics and Sysmex® Coagulation Systems. The INNOVANCE® D-Dimer assay is intended for use in conjunction with a non-high clinical pre-test probability (PTP) assessment model to exclude deep vein thrombosis (DVT) and pulmonary embolism (PE).

**E. System Descriptions:**

1. Device (Instrument) Description:

The Sysmex CS-2100i is an automated blood coagulation instrument for in vitro diagnostic use in clinical laboratories. The instrument analyzes venous plasma samples collected in 3.2% sodium citrate using clotting, chromogenic and immunoassay methods. Analysis results are displayed on the Information Processing Unit (IPU) screen. Results can be printed on external printers or transmitted to a host computer. The instrument is capable of measuring the assays in a normal mode and a micro-sample mode.

For the previously cleared assay description refer to K151259 and K093626.

2. Principles of Operation:

The Sysmex CS-2100i is an automated blood coagulation instrument which performs testing analysis using its mechanical, hydraulic, and electrical systems. The instrument uses associated reagents, controls, calibrators, and consumable materials to perform assays for Prothrombin Time (PT) seconds and PT INR, Activated Partial Thromboplastin Time (APTT), Fibrinogen, Antithrombin, and D-dimer.

3. Modes of Operation:

Random access, open tube or capped vials.

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

Yes  or No

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

Yes  or No

4. Specimen Identification:

Specimens can be identified either manually or by barcode:

5. Specimen Sampling and Handling:

- a. Normal mode: Automatic pipetting of a specimen; capped sample tube analysis and re-analysis.
- b. Micro mode: Automatic pipetting of a specimen for each analysis through a secondary dispensing sample probe; sample tubes must be uncapped; no automatic re-analysis.

6. Calibration:

Calibration is an automated function of the Sysmex CS-2100i coagulation analyzer. A calibration curve is performed for each calibrated application.

7. Quality Control:

The analyzer has two types of control methods: X-Bar control and Levey-Jennings control.

8. Software:

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

Yes \_\_\_\_\_ X \_\_\_\_\_ or No \_\_\_\_\_

**F. Regulatory Information:**

1. Regulation section:

21 CFR 864.5425, Multipurpose system for in vitro coagulation studies

2. Classification:

Class II

3. Product code:

JPA, System, multipurpose for in vitro coagulation studies

4. Panel:

Hematology (81)

**G. Intended Use:**

1. Indication(s) for Use:

The Sysmex CS-2100i is a fully automated blood coagulation analyzer intended for in vitro diagnostic use using venous blood samples collected 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.

2. Special Conditions for Use Statement(s):

For prescription use only.

**H. Substantial Equivalence Information:**

1. Predicate Device Name(s) and 510(k) numbers:

Sysmex® CA-1500 (K011235)

2. Comparison with Predicate Device:

The predicate system is the INNOVANCE D-dimer assay DVT exclusion claim using the Sysmex CA®-1500.

<b>Similarities</b>		
Item	Device Sysmex CS-2100i	Predicate Sysmex CA®-1500
Intended Use	<p>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:</p> <ul style="list-style-type: none"> <li>• Prothrombin Time (PT) seconds and PT INR with Dade® Innovin®</li> <li>• Activated Partial Thromboplastin Time (APTT) with Dade® Actin® FSL</li> <li>• Fibrinogen (Fbg) with Dade® Thrombin Reagent</li> <li>• Antithrombin (AT) with INNOVANCE® Antithrombin</li> <li>• D-dimer with INNOVANCE® D-Dimer</li> </ul> <p>The performance of this device has not been established in neonate and pediatric patient populations.</p>	<p>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:</p> <p>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.</p> <p>Chromogenic Analysis Parameters: Antithrombin III; Factor VIII; Plasminogen; Heparin; Protein C; α2-Antiplasmin.</p> <p>Immunologic Analysis Parameters: D-dimer.</p> <p>Calculated Parameters: PT</p>

<b>Similarities</b>		
<b>Item</b>	<b>Device Sysmex CS-2100i</b>	<b>Predicate Sysmex CA®-1500</b>
		Ratio; PT INR; PT %; Derived Fibrinogen; Factor Assays % Activity
Application	Immuno-chemical Application: D-dimer with INNOVANCE® D-Dimer	Same
Sample Type	3.2% sodium citrate venous plasma	Same
Clinical Reportable Range	0.19 to 35.2 mg/L FEU	Same
Specimen Processing	Automatic Pipetting and Dilution	Same
Sampling Mode	Normal and Micro Mode	Same
Sample Volumes in Normal Mode	13 µL	Same
Temperature Control	Sample incubation well: 37°C ± 1.0°C	Same
Random Access	Yes	Same
Liquid Level Sensing	Yes – reagent and sample	Same
Bar Code Reader	Sample + reagent	Same
Rinse & Buffer Solutions - On-board - External	CA-CLEAN I; CA-CLEAN II; Dade Owren's Buffer Water	Same Same
STAT Testing	Yes	Same

<b>Differences</b>		
<b>Item</b>	<b>Device Sysmex CS-2100i</b>	<b>Predicate Sysmex CA®-1500</b>
Operating Principle: Immuno-chemical	D-dimer at 660 nm	D-dimer at 800 nm
Light Source:	Halogen Lamp	Light Emitting Diode
Cap Piercing	Cap piercer	Cap piercer and No cap piercer
Pipetting Capabilities - Reagent probe - Sample probe	20 – 200 µL 4 – 270 µL	3 – 200 µL 5 – 450 µL
Temperature Control	-Detector : 37°C ± 0.5°C -Reagent incubation probe : 37.5 °C ± 0.5 °C	-Detector: 37°C ± 1.0°C -Reagent incubation probe: 37°C ± 1.0°C

<b>Differences</b>		
<b>Item</b>	<b>Device Sysmex CS-2100i</b>	<b>Predicate Sysmex CA®-1500</b>
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
Sample Volumes in Micro Mode	15 µL	13 µL
Bidirectional Interface Communication Protocols	CA-, ASTM-, CS- Protocol	CA-, ASTM-Protocol

**I. Special Control/Guidance Document Referenced (if applicable):**

CLSI H59-A Quantitative D-dimer for the Exclusion of Venous Thromboembolic Disease

**J. Performance Characteristics:**

1. Analytical Performance:

Applicable analytical performance studies using the INNOVANCE® D-Dimer assay on the Sysmex CS-2100i are documented in K151259. The following studies were performed and were not necessary to reproduce for this submission because the performance remains unchanged: method comparison with predicate device, clinical cut-off validation for pulmonary embolism (PE), precision/reproducibility, linearity, detection limit, carryover, interfering substances, on-board stability for reagent and control material, ambient temperature tolerance testing, expected values/reference range, dilution options comparison, and normal mode vs. micro mode comparison.

2. Other Supportive Instrument Performance Data Not Covered Above:

Clinical cut-off: Validation for deep vein thrombosis (DVT)

The INNOVANCE® D-Dimer assay was evaluated on the Sysmex CS-2100i analyzer in a multi-center study at U.S. and foreign (European) sites to validate the exclusion of a first event of deep vein thrombosis (DVT). These sites were emergency or ambulatory departments.

All potentially eligible patients who were suspected of having a first event DVT were evaluated using the Wells' rules to estimate their pre-test probability (PTP), 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 each study center were

evaluated by imaging methods . Patients with a negative D-dimer result with the D-dimer assay used at each 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.

Specimens were collected prospectively from 1907 consecutive outpatients and stored frozen. Of these 1907 patients, 368 were excluded from analysis based on the pre-analytical and post-analytical exclusion criteria (including 213 patients reported to have a previously documented or chronic DVT), resulting in a total of 1539 patients. In addition, patients with unobtainable follow-up data were excluded from analysis resulting in 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 U.S. patients and 4.7 % in the European patients.

The specimens collected in clinical sites were tested with the INNOVANCE® D-Dimer assay on the Sysmex CS-2100i analyzer 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. 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:

Clinical Sensitivity and Specificity; U.S. Results

U.S. sites DVT		Reference (Imaging and 3-month follow-up)		
		Positive	Negative	Total
INNOVANCE® D-Dimer on Sysmex CS- 2100i System	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

U.S. prevalence = 56/803 = 0.070 = 7.0%

\*standardized to a prevalence of 15%

Clinical Sensitivity and Specificity; Outside U.S. Results (OUS)

OUS sites DVT		Reference (Imaging and 3-month follow-up)		
		Positive	Negative	Total
INNOVANCE® D-Dimer on Sysmex CS- 2100i System	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

OUS prevalence = 24/514 = 0.047 = 4.7 %

\*standardized to a prevalence of 15%

Clinical Sensitivity and Specificity; Overall Results

U.S. and OUS sites DVT		Reference (Imaging and 3-month follow-up)		
		Positive	Negative	Total
INNOVANCE® D-Dimer on Sysmex CS- 2100i System	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

U.S. + OUS prevalence = 80/1317 = 0.061 = 6.1 %

\*standardized to a prevalence of 15%

**K. Proposed Labeling:**

The labeling is sufficient and does satisfy the requirements of 21 CFR Part 809.10.

**L. Conclusion:**

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