510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM

A. 510(k) Number:

K170960

B. Purpose for Submission:

New device

C. Measurand:

International Normalized Ratio (INR)

D. Type of Test:

Electrochemical technology with amperometric (electric current) detection of thrombin activity

E. Applicant:

Roche Diagnostics, Inc.

F. Proprietary and Established Names:

CoaguChek® Vantus System and CoaguChek XS PT Test Strips

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.7750, Prothrombin time test

2. Classification:

   Class II

3. Product code:

   GJS, Test, time, prothrombin

4. Panel:

Hematology (81)

H. Intended Use:

1. Intended use(s):

   The CoaguChek Vantus System measures an INR (International Normalized Ratio) based on a prothrombin time (PT) response to monitor the effect of a therapy with vitamin K antagonists by using the CoaguChek XS PT test strips. The CoaguChek Vantus System uses fresh capillary whole blood from a finger stick.

   The system is intended for properly selected and suitable trained users on the prescription of the treating doctor.

   Users should be stabilized on anticoagulation with vitamin K antagonists for at least 6 weeks prior to single patient self-testing with the CoaguChek Vantus System.

   The CoaguChek Vantus System is intended for single patient self-testing only for adults, age 22 years and older.

2. Indication(s) for use:

   Same as intended use

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   CoaguChek Vantus meter

I. Device Description:

The CoaguChek Vantus System consists of a hand-held CoaguChek Vantus meter, used in combination with the CoaguChek XS PT test strips. The CoaguChek Vantus meter is a small handheld instrument intended for the quantitative measurement of INR based on a PT response by using a single electrochemical test strip. The CoaguChek XS PT test strip contains a lyophilized reagent (reagent in dried form). The reactive components of this reagent consist of thromboplastin and a peptide substrate.

The test strip has one reaction chamber, which includes both the prothrombin time reaction and on-board quality control (OBC). The prothrombin time test reaction and OBC tests run simultaneously, which are based on electrochemical technology. If the quality control are within limits, the strip integrity is verified. If the OBC is not within limits, the meter displays an according error and the test result is not reported.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   CoaguChek XS System

2. Predicate 510(k) number(s):

   K062925

3. Comparison with predicate:

Similarities		
Item	Device CoaguChek Vantus System K170960	Predicate CoaguChek XS System K062925
Intended Use/ Indications for Use	The CoaguChek Vantus System measures an INR (International Normalized Ratio) based on a prothrombin time (PT) response to monitor the effect of a therapy with vitamin K antagonists by using the CoaguChek XS PT test strips. The CoaguChek Vantus System uses fresh capillary whole blood from a fingerstick. The system is intended for properly selected and suitable trained users on the prescription of the treating doctor. Users should be stabilized on anticoagulation with vitamin K antagonists for at least 6 weeks prior to single patient self-testing with the CoaguChek Vantus System. The CoaguChek Vantus System is intended for single patient self-testing only for adults, age 22 years and older.	The CoaguChek XS PT test strips are part of the CoaguChek XS System. The CoaguChek XS System measures blood clotting time for people who are taking anticoagulation medications such as Coumadin or warfarin. The CoaguChek XS System uses blood from a finger stick. The system is intended for properly selected and suitably trained users or their caregivers on the prescription or other order of the treating doctor. Users should be stabilized on anticoagulation medications such as Coumadin or warfarin prior to self- testing with the CoaguChek XS System.
Test Strip	CoaguChek XS PT test strip	Same
Sample Type	Capillary whole blood	Same
Operating Principle	Electrochemical technology with amperometric (electric current) detection of thrombin activity	Same
Reagent Test Strip Principle	Human recombinant thromboplastin	Same
Sample Volume	Minimum of 8µL	Same

Similarities		
Item	Device CoaguChek Vantus System K170960	Predicate CoaguChek XS System K062925
On Board Controls	Built into each CoaguChek XS PT test strip	Same
Hematocrit Range	Hematocrit ranges between 25 – 55% have no significant effect on test results	Same
Bilirubin	Bilirubin up to 30 mg/dL have no significant effect on test results	Same
Triglyceride	Lipemic samples containing up to 500 mg/dL of triglycerides have no significant effect on test results	Same
Hemolysis	Hemolysis up to 1000 mg/dL have no significant effect on test results	Same
Heparin	Test results are unaffected by heparin concentrations up to 0.8 U/mL	Same
Low Molecular Weight Heparin	CoaguChek XS PT test strip is insensitive to low molecular weight heparins (LMWH) up to 2 IU anti-factor Xa activity/mL	Same

Differences		
Item	Device CoaguChek Vantus System K170960	Predicate CoaguChek XS System K062925
Measuring Range	0.8 to 6.0 INR	0.8 to 8.0 INR
Memory Capacity	300 test results with date and time Code chip data from up to 5 test strip lots can be stored	300 test results with date and time No test strip lot information stored (code chip data)
Communication interface	Bluetooth, USB	Infrared

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

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition

CLSI EP07-A2: Interference Testing in Clinical Chemistry

CLSI EP47-A2: One-stage Prothrombin Time (PT) Test And Activated Partial

Thromboplastin Time (APTT) Test

IEC 60601-1-2 Edition 3: 2007-03, medical electrical equipment - part 1-2: general requirements for basic safety and essential performance - collateral standard: electromagnetic compatibility - requirements and tests

IEC 61010-1 Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1 General Requirements

IEC 61010-2-101:2015 Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-101: Particular requirements for laboratory equipment for in vitro diagnostic (IVD) medical equipment

L. Test Principle:

When a blood sample is applied to the test strip, thromboplastin activates the coagulation cascade which leads to the formation of thrombin. The activity of thrombin, the final protease for both plasmatic coagulation pathways, is monitored during the test instead of detecting the clot by mechanical or optical methods. Thrombin cleaves the thrombin substrate creating an electrochemically active peptide, which generates an electrical signal. The signal is converted to a PT/INR value and displayed by the CoaguChek Vantus meter.

The CoaguChek Vantus System connects with the CoaguChek® XS PT test strip by means of seven main electronic pins. These contact points allow the CoaguChek Vantus meter to generate and display valid PT/INR results even if there are minor defects on the test strip (e.g. small scratches).

CoaguChek Vantus uses the identical electrochemical technology as the CoaguChek XS System to perform the PT test and the on-board quality control (OBC) test simultaneously. The OBCchecks the test strip integrity for damage from extreme temperature, humidity or light. The chemical components of the OBC are added directly to the formulation of the thromboplastin reagent. This ensures that the check for the test strip integrity is performed for every single strip at the same place and same time as the PT test ("on the spot OBC"). The test system determines whether the OBC result is within preset limits, if it is, then the strip integrity is verified, and the meter reports the PT test. If the OBC is not within limits, the meter displays an error and a test result is not reported. Release testing during manufacturing determines and sets the lot-specific ranges for the OBC.

M. Performance Characteristics (if/when applicable):

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

   a. Precision/Reproducibility:

      i. Repeatability with fresh capillary whole blood:

The repeatability study was performed at four study sites, with 16 CoaguChek Vantus instruments, three lots of CoaguChek XS PT test strips and at least two operators per site. A total of 688 fresh capillary whole blood specimens from subjects on oral anticoagulation therapy with vitamin K antagonists and healthy subjects were obtained. The repeatability results passed the acceptance criteria. The table below shows the repeatability results for combined sites.

Range [INR]	No. of samples (n=2)	Mean [INR]	SD	Upper 95% CI of SD	CV [%]	Upper 95% CI of CV
<2.0	200	1.1	0.04	0.05	3.8	4.2
2.0 – 3.5	394	2.6	0.08	0.09	3.1	3.2
>3.5 – 4.5	70	4.0	0.12	0.14	3.2	3.7
>4.5 – 6.0	24	4.9	0.07	0.10	1.5	2.0
All	688	2.4	0.08	0.08	3.3	3.4

ii. Intermediate Precision (Reproducibility):

The intermediate precision study was performed over the course of 20 days using four levels of control material, with duplicates of each sample tested twice a day. This study was performed at four study sites, with 39 CoaguChek Vantus instruments, and three lots of CoaguChek XS PT test strips. Site 1 had two operators, site 2 had one operator, site 3 had two operators and site 4 had three operators. The following components of variability for each level of control were determined and are shown below: within-run, between-run, between-day, and total (intermediate precision) precision. The CoaguChek Vantus System demonstrated acceptable results when evaluated using control material at four levels spanning the reportable range of the device.

			Repeatability (Within Run)		Between Run		Between Strip Lot		Between Day		Between Site		Reproducibility	
Control Level	N	Mean	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	1040	1.32	0.03	2.4	0.01	0.6	0.04	2.9	0.01	0.7	0.01	1.0	0.05	4.0
2	1040	2.79	0.11	4.0	0.00	0.0	0.02	0.7	0.00	0.0	0.03	1.0	0.12	4.2
3	708	5.85	0.17	2.9	0.07	1.2	0.14	2.3	0.04	0.8	0.02	0.4	0.24	4.0
4	712	3.39	0.09	2.7	0.04	1.2	0.03	1.0	0.00	0.0	0.03	0.9	0.11	3.2

b. Linearity/assay reportable range:

i. Linearity: Not applicable

ii. Assay Reportable Range: The assay reportable range (0.8 – 6.0 INR) of the CoaguChek Vantus System was established through method comparison studies against both the predicate (Roche CoaguChek XS System) and the reference device (Sysmex CA-1500 laboratory analyzer using Dade Innovin Reagent).

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

i. Traceability: Each lot of CoaguChek XS PT test strips is factory calibrated to a reference lot of human recombinant thromboplastin traceable to the WHO International Reference Preparation, rTF/95.

ii. Closed Vial and Transport Stability: The CoaguChek XS PT test strips were stored at 2–8°C and 26–30°C and tested after a storage time of 3, 6, 16 and 25 months.

iii. Open Vial Stability: Open vial stability simulates the repeated opening and closing of the vial by the customer when test strips are removed from the vial for measurement. Open vial stability was tested by opening the vials once per day for at least one minute at 32°C, 85% relative humidity (RH) over a period of 30 days.

iv. Out of Vial Stability: Out of vial stability was tested to demonstrate that the test strips can be kept outside the vial before measurement for at least 10 minutes when directly exposed to 32°C, 85% RH. This was verified by storing the test strip outside the vial under the specified environmental conditions for 14 minutes before measurement.

d. *Detection limit:*

Factor sensitivity was assessed for coagulation factors II, V, VII and X using four lots of CoaguChek XS PT test strips. The factor sensitivity was performed using standard human plasma that was mixed with varying amounts of factor II, V, VII and X deficient plasma to obtain plasma samples with different factor activities (0, 1, 19, 20, 30, 40, 50, 60, 70, 80, 90 and 100%). For each CoaguChek XS PT test strip, four measurements were performed per coagulation factor and dilution level. The study verifies factor sensitivity for the CoaguChek XS PT test strips at the following levels: Factor II < 31%; Factor V < 46%; Factor VII < 44%; and Factor X < 50%.

e. *Analytical specificity:*

The interference studies were performed for the following interferents: bilirubin, hemolysis, heparin, LMWH and triglycerides. In addition, an interference study was conducted to characterize the levels of other known drugs: oritavancin, daptomycin, clopidogrel, fondaparinux, rivaroxaban, apixaban, dabigatran and edoxaban.

Interference limits were established using up to four CoaguChek XS PT test strip lots, using fresh citrated venous whole blood from both normal and warfarin blood samples spiked separately with the interferents. The acceptance criteria for interference effect of the aforementioned interferents were met. The interference study results demonstrate that the following interferents do not interfere with test results up to following concentrations:

Interferent	Concentration
Bilirubin	Up to 30mg/dL
Hemolysis	Up to 1000 mg/dL
Heparin	Up to 0.8 U/mL
Low Molecular Weight Heparin	Up to 2 IU anti-factor XA activity/mL
Triglycerides	Up to 500 mg/dL
Clopidogrel	Up to 20 mg/dL
Fondaparinux	Up to 0.5 mg/L
Oritavancin	Cannot be tested with the system
Daptomycin	Up to 50 mg/L
Rivaroxaban	Cannot be tested with the system
Apixaban	Cannot be tested with the system
Dabigatran	Cannot be tested with the system
Edoxaban	Cannot be tested with the system

Hematocrit

The hematocrit interference study was conducted with one lot of CoaguChek XS PT test strips on the CoaguChek Vantus meter using venous whole blood samples from three healthy donors and 10 VKA treated donors adjusted to the following hematocrit values: 0%, 15%, 30%, 45% and 55%. To achieve the desired hematocrit values, centrifugation was utilized and at least four measurements were performed per sample. Results demonstrated that the CoaguChek XS PT test strip is unaffected by hematocrits within the claimed hematocrit range of 25–55%.

f. Assay cut-off

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Accuracy was evaluated by comparing the CoaguChek Vantus System against the predicate device, CoaguChek XS System. The method comparison study was performed using capillary whole blood samples from subjects not receiving warfarin and from subjects on warfarin therapy. The method comparison study was conducted across four point-of-care sites using three CoaguChek XS PT test strip lots. The table below summarizes the study results by individual sites and combined sites.

CoaguChek Vantus INR versus CoaguChek XS INR

Statistic	Site 1	Site 2	Site 3	Site 4	All Sites
Slope (95% CI)	1.00 (1.00, 1.00)	1.00 (1.00, 1.09)	1.06 (1.00, 1.10)	1.00 (1.00, 1.07)	1.00 (1.00, 1.00)
Intercept (95% CI)	0.1 (0.1, 0.1)	0.1 (-0.2, 0.1)	-0.1 (-0.2, 0.1)	0.1 (-0.1, 0.1)	0.1 (0.1, 0.1)
Pearson (r)	0.99	0.98	0.99	0.98	0.99
Total Samples	67	43	49	48	207

Method Comparison with reference device:

Accuracy was also evaluated by comparing the INR results of capillary samples measured on the CoaguChek Vantus System to the INR of venous plasma measured on the Sysmex CA 1500 laboratory analyzer using the Dade Innovin recombinant human tissue thromboplastin reagent. The method comparison study was performed across four sites using three CoaguChek XS PT test strip lots. The data from individual sites were combined and a Passing-Bablok regression analysis was performed. The following table summarizes the study results from individual sites and combined sites.

CoaguChek Vantus INR versus Innovin INR

Site	N	Slope (95% CI)	Intercept (95% CI)	Pearson (r)
All	200	0.98 (0.93, 1.03)	0.1 (0.0, 0.3)	0.91
1	67	0.94 (0.85, 1,02)	0.2 (-0.0, 0.4)	0.86
2	43	1.02 (0.92, 1.15)	0.1 (-0.2, 0.3)	0.97
3	47	1.03 (0.94, 1.12)	0.0 (-0.2, 0.2)	0.97
4	43	0.95 (0.82, 1.13)	0.2 (-0.3, 0.5)	0.93

b. *Matrix comparison:*

Not applicable

3. Clinical studies:

a. *Clinical Sensitivity:*

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Home Use Study

This study compared test results obtained by self-testers on the CoaguChek Vantus system to results obtained by self-testers on the CoaguChek XS System (self-tester owned). Self-testers did not receive formal training on the CoaguChek Vantus System prior to the study. The self-tester performed at least 10 INR measurements with the CoaguChek Vantus System in their home, spanning at least 10 days. The following table summarizes the study results.

N	Slope (95% CI)	Intercept (95% CI)	Pearson (r)
134	1.00 (1.00, 1.03)	0.00 (0.00, 0.00)	0.94

Self-testers enrolled in the study also participated in a questionnaire to survey the usability of the CoaguChek Vantus system. On a scale of 1 to 5 where 1 is most favorable and 5 is least favorable, the mean score was 1.4.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

A normal range study was conducted on 121 healthy subjects not on anticoagulation therapy. Capillary whole blood sample testing performed on the subjects not on VKA therapy demonstrated that 95% of the INR results ranged between 0.9–1.1.

N. Instrument Name:

CoaguChek Vantus System

O. System Descriptions:

1. Modes of Operation:

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

Yes ___X____ or No _____

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

Yes ___X_____ or No _____

2. Software:

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

   Yes ___X_____ or No _____

3. Specimen Identification:

   Code chip contains information about the test method, the lot number and the expiry date. The date and INR result is recorded by the CoaguChek Vantus meter.

4. Specimen Sampling and Handling:

   The CoaguChek XS PT test strip is intended for single-use only. Once the test strip is inserted into the meter, a drop of fresh capillary whole blood sample collected by a fingerstick is manually applied to the test strip target area and analyzed by the CoaguChek Vantus meter.

5. Calibration:

   Each lot of CoaguChek XS PT test strips is factor calibrated to a reference lot of human recombinant thromboplastin traceable to the World Health Organization International Reference Preparation. This lot-specific calibration information is embedded within the code chip, which is required by the CoaguChek Vantus meter prior to using the specific lot of the CoaguChek XS PT test strip.

6. Quality Control:

   The CoaguChek Vantus System provides On-Board Controls (OBC), which provide a quality control check for each individual CoaguChek XS PT test strip used with the CoaguChek Vantus meter. There are no additional steps required by the user to activate the OBC.

   When a test strip is inserted, the CoaguChek Vantus meter, the first check assesses potential issues with the reagent. The second check ensures that the test strip has not been exposed to environment conditions or physical stresses, like bending. If either of these checks do not pass, then no INR result is provided.

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

Temperature and Altitude Study: The purpose of this study was to examine the specified operating temperature and humidity conditions for the CoaguChek XS PT test strip on the CoaguChek Vantus instrument. Using the CoaguChek XS PT test strip, operating temperature range was evaluated using two different levels of CoaguChek XS PT Controls over the specified temperature range of 15–32°C (59–90°F) and the specified relative humidity (RH) range of 10–85%. Additional temperature conditions were also tested in combination with 60% RH: 9°C, 12°C, 23°C, 34°C and 36°C. Results from these studies met the acceptance criteria and demonstrated that the performance of the CoaguChek XS PT test strip on the CoaguChek Vantus instrument is not affected by operating temperatures under the conditions specified above.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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