

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

K060978

B. Purpose for Submission:

Clearance of a new instrument and test strip

C. Measurand:

Prothrombin Time

D. Type of Test:

Electrochemical

E. Applicant:

Roche Diagnostics Corporation

F. Proprietary and Established Names:

CoaguChek® XS System

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7750

2. Classification:

Class II

3. Product code:

GJS

4. Panel:

H. Intended Use:

1. Intended use(s):

The CoaguChek® XS System is intended for use by professional healthcare providers for quantitative prothrombin time testing for the monitoring of warfarin therapy. The CoaguChek® XS System uses fresh capillary or non-anticoagulated venous whole blood.

2. Indication(s) for use:

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

The CoaguChek® XS System includes a meter and CoaguChek® XS PT test strips. The test strip contains a human recombinant tissue factor, and is calibrated to an ISI of 1.0.

The test strip incorporates quality control material that accesses strip integrity.

The CoaguChek® XS meter automatically stores up to 100 test results along with their dates and times in memory.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche Diagnostics CoaguChek S System

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

K020831

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative prothrombin time (PT) using fresh capillary or non-anticoagulated venous whole blood	same
Measuring Range	0.8- 8.0 INR	Same
Sample Volume	10 µl	same
Reagent	Human recombinant thromboplastin	same

Differences		
Item	Device	Predicate
Technology	Electrochemical with amperometric detection of thrombin activity	Optical detection of thrombin activity
Quality Control	On-board integrated QC which detects test strip integrity	External liquid controls and electronic quality control
Test Strip Dosing	Top and side dosing	Top dosing only
Memory	100 test results with time and date	60 test results with time and date

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

NCCLS/CLSI Document C28-A, “How to Define and Determine Reference Intervals”

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. Thrombin cleaves the thrombin substrate creating an electrochemically active peptide, which generates an electrical signal. The signal is converted to an INR value and displayed by the CoaguChek XS System.

The on-board quality control is a bi-level control that accesses test strip integrity. The PT test and QC testing are performed simultaneously. The test system determines whether the quality control is within preset limits. If it is, the meter displays a short term “QC✓”, and then the PT test result. If the QC is not within limits, the meter displays “error QC”, and no PT test result will be displayed.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision was evaluated by performing duplicate measurements of both capillary and venous blood. The acceptance criteria for venous blood was $\leq 4.5\%$ INR and $\leq 7.5\%$ INR for capillary samples. Testing was performed on two lots of test strips and demonstrated acceptable performance.

b. *Linearity/assay reportable range:*

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

d. *Detection limit:*

e. *Analytical specificity:*

Testing demonstrated no interference with unfractionated heparin up to 2 u/ml from normal donors, and up to 0.8 u/mL for warfarin patients. Acceptance criteria was $\leq 10\%$ difference when compared to the unspiked sample.

Tinzaparin and Enoxaprin (LMWH's) showed no interference up to 2 IU anti-Xa activity/ml for both normal donors and warfarin patients. Acceptance criteria was $\leq 10\%$ difference when compared to the unspiked sample.

Testing was performed to demonstrate the interference of bilirubin, lipemia, and hemolysis. Results showed no interference from bilirubin up to 30 mg/dL, lipemia up to 500 mg/dL, and hemolysis up to 1000 mg/dL. Acceptance criteria was $\leq 10\%$ difference when compared to the unspiked sample.

f. *Assay cut-off:*

2. Comparison studies:

a. *Method comparison with predicate device:*

Study involving 361 patients (43% female, 57% male) at 3 sites. Clinical conditions include normal -not on warfarin (63), atrial fibrillation (175), valve replacement (36), stroke/TIS (28), DVT (16), other heart-related disorders (4), other clotting disorders (6), other (33). Two lots of test strips, on two meters were used. Results were compared to a Dade Innovin® thromboplastin (ISI =1.02) assayed on a Sysmex® analyzer. Bias plots were presented to demonstrate bias with a laboratory plasma method. Acceptance criteria was ≤ 0.5 INR difference to lab INR for INR's in the range of 0.8 to 2.9, and $\leq 30\%$ difference to lab INR for INR's in the range of 2.0 to 4.5. Data demonstrated acceptable results for all sites.

Regression analysis was presented for the entire data set (venous $y = 1.034x - 0.02$, Slope CI 1.017-1.053, Int CI -0.04-0.01, $r = 0.974$, $n = 710$; capillary $y = 1.006x + 0.032$, Slope CI 0.990-1.023, Int CI -0.01-0.06, $r = 0.971$, $n = 700$) and each site across the reportable range. The regression analysis for the entire data set is included in the package insert.

b. Matrix comparison:

Regression analysis was presented to compared capillary versus venous results by site, and combined for two lot of test strips. Lot 1 ($y = 0.97x + 0.033$; $y = 1.00x + 0$; $y = 0.97x + 0.047$ / $y = 0.98x + 0.023$) and Lot 2 ($y = 1.00x + 0$; $y = 1.00x + 0$; $y = 1.00x + 0$ / $y = 1.00x + 0$) both meet the acceptance criterion (slope 0.95-1.05, intercept of ± 0.1).

3. Clinical studies:

a. Clinical Sensitivity:

b. Clinical specificity:

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

4. Clinical cut-off:

5. Expected values/Reference range:

Normal range testing was conducted on 121 patients who were not on oral anticoagulant therapy. Both capillary and venous samples were collect from each patient. Samples

were tested on two lots of CoaguChek XS PT strips. Results demonstrated a normal range of 0.9 to 1.1 INR with more than 95% of all results falling within that range.

N. Instrument Name:

CoaguChek XS meter

O. System Descriptions:

1. Modes of Operation:

Manual, closed system

2. Software:

The CoaguChek XS software controls the user interface, buttons used to navigate the user interface and to configure the device, storage of patient results, transfer of measurement results using serial infrared communication in an open mode, transfer of production and calibration results using serial infrared communication in a protected mode, reading and storage of specific information for strip LOT from code key, calculation of PT time based on data received from measurement cycle, and checks for failsafe in order to recognize malfunctions of the measurement electronics or malfunctions within the strip used for testing.

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

Yes or No

3. Specimen Identification:

Date and time of testing is recorded by the CoaguChek XS meter

4. Specimen Sampling and Handling:

Whole blood is manually applied to the target area of the test strip either from the top or side of the strip.

5. Calibration:

The CoaguChek XS Test strips are calibrated to a master reagent lot which has in turn been calibrated to a WHO International Reference Preparations (rTF/95) using the manual tilt tube method.

6. Quality Control:

The CoaguChek XS System incorporates a bi-level on-board quality control (OBC) within the CoaguChek XS test strip that monitors test strip integrity.

Level 1 OBC detects strip defects such as reagent defects, capillary compression and electrode defects. Level 2 OBC directly measures strip damage due to such things as exposure to increased humidity, light, and temperature.

The pre-determined OBC ranges are programmed into the lot specific code chip that is packaged with the matching test strip lot.

Acceptable data was presented validating the OBC.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In the “Performance Characteristics” Section above:

An instrument failsafe checklist was presented outlining the QC check made by the CoaguChek XS meter.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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

