

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

A. 510(k) Number:

K050243

B. Purpose for Submission:

To obtain clearance for the Immedia™ Prothrombin Time System

C. Measurand:

Prothrombin Time

D. Type of Test:

Quantitative clotting assay

E. Applicant:

Farallon Medical, Inc.

F. Proprietary and Established Names:

Immedia™ Prothrombin Time System

G. Regulatory Information:

1. Regulation section:

21 CFR 864.5425

2. Classification:

Class II

3. Product code:

JPA

4. Panel:

H. Intended Use:

1. Intended use(s):

The Immedia Prothrombin Time System is an *in vitro* diagnostic device that provides quantitative prothrombin time (PT) results, expressed in seconds and INR units. It uses fresh capillary whole blood. It is intended for use by health care professionals at the point of care to monitor patients who are on warfarin-type (coumarin) anticoagulation therapy. This device is not intended to be used for screening purposes.

2. Indication(s) for use:

The Immedia System is intended for use by health care professionals at the point of care to monitor patients who are on warfarin-type (coumarin) anticoagulation therapy. This device is not intended to be used for screening purposes.

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

The Immedia Prothrombin Time System measures the Prothrombin Time (PT) of fresh capillary whole blood. The test is performed by inserting a test strip into the meter and applying a drop of blood to the sample receptacle of the test strip. The meter automatically performs the PT test and the result is displayed as International Normalized Ratio (INR) and seconds (PT). The meter automatically stores all test results in memory. The device is powered by batteries and/or AC adapter. The disposable test strip contains a rotating, spoked wheel that draws the sample into the reaction well after it is applied to the sample receptacle. The spokes rotate across the path of an infrared light beam and mix the liquid sample with the dried thromboplastin in the reaction well. A separate Calibration Strip is used to input calibration data. High Control and Low Control Strips are provided for quality control purposes.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Roche CoaguChek S System

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

K994349

3. Comparison with predicate:

| Similarities | | |
|---------------------|---|--|
| Item | Device | Predicate |
| | Farallon Immedia System | Roche CoaguChek S System |
| Methodology | Quantitative PT testing by detection of thromboplastin-initiated activity in the extrinsic coagulation pathway | Same |
| Hematocrit Range | Ranges between 32-52% do not significantly affect test results | Same |
| Storage Conditions | Test Strips: Refrigerate at 2-8 °C until ready to use. Prior to opening, the strip should be at room temp, (18-32 °C). Strips may be stored at room temp for 60 days. Meter Operation: 18-32 °C, 10-75% relative humidity without condensation | Same 18-32 °C, less than 85% relative humidity without condensation |

| Differences | | |
|--------------------|--|---|
| Item | Device | Predicate |
| Test Principle | Rotating wheel physically lifts the clot at the time coagulation occurs and is detected by interruption of infrared light beam | Detects clot formation with iron particles in a magnetic field |
| Reagent | Dried recombinant thromboplastin | Non-human thromboplastin |
| Calibration | User inserts calibration strip containing the bar coded calibration information into the meter. CAL strip supplied with each carton of test strips | User inserts a code chip, supplied with each box of test strips into meter |
| Quality Control | Each carton of test strips contains control strips (containing thromboplastin with low/high level of plasma) to be tested at start of each new carton of strips, when PT results are suspect, or daily startup | Users are directed to perform daily electronic quality control testing and liquid control testing with each new shipment and/or lot of test strips or when test results are suspect |

| Differences | | |
|-------------------|---|---|
| Item | Device | Predicate |
| Meter Storage | -25 to 50 °C, 10-90% relative humidity without condensation | -25 to 70 °C, 10-90% relative humidity without condensation |
| Measurement Range | 0.8 – 8.0 INR | 0.6 – 8.0 INR |

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

L. Test Principle:

The Immedia™ Prothrombin Time System operates by a rotating wheel drawing in the drop of sample to the reaction well after it is applied in the sample receptacle. The reaction well contains a pre-measured and dried-on quantity of thromboplastin. The wheel spokes rotate across the path of an infrared light beam. The spokes mix the patient sample with the reagent. As the patient sample transforms into a solid clot, it is picked up by the continuously-rotating spokes and is carried across the path of the infrared light beam interrupting the beam pattern.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Testing was performed at the following clinical sites: Loma Linda VA Medical Center, Loma Linda, CA; Lovelace Medical Center, Albuquerque, NM; Palo Alto Medical Foundation Palo Alto, CA. Reference testing was conducted at Hemostasis Reference Labs, Henderson Research Center, Hamilton, Ontario, Canada.

a. Precision/Reproducibility:

Control precision – On each day of testing at the three sites during the clinical trial, two levels of control (22 low and 23 high control samples) were tested on both the Immedia PT System and CoaguChek S devices.

Low Control: Mean PT/INR: 17.6 / 1.4 %CV: PT- 3.9 INR- 6.2

High Control: Mean PT/INR: 32.5 / 3.5 %CV: PT-3.5 INR- 5.4

Therapeutic samples precision - studies were conducted on the 30 replicate samples of citrated plasma and whole blood recalcified with 250 mM calcium chloride and tested on the Immedia PT System.

Sample 1(whole blood): Mean PT/INR: 24.4 / 2.4 % CV: PT-2.7 / INR-4.3

Sample 2 (plasma): Mean PT/INR: 32.2 / 3.7 % CV: PT-3.3 / INR-5.2

Capillary whole blood precision - At one clinical study site, 30 subjects were tested in duplicate over the measuring range on the Immedia PT System.

Mean PT/INR: 24.7 / 2.4 %CV: PT - 2.6 / INR - 3.5

b. Linearity/assay reportable range:

Linearity testing was done according to CLSI EP6-A guidance. Plasma of known INR was purchased from Research Protein, Inc. 12 μ L of each was mixed with 0.75 μ L of 250 mM calcium chloride. Duplicates of the diluted Fixed INR Plasma samples were tested on the Immedia PT System and then tested using the ACL 100 following the manufacturer's operating instructions. The mean PT and INR values obtained from the Immediate PT System meter were plotted versus the assigned values. The Immedia System was found to be linear up to an INR of 8.0.

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

Stability testing was performed on the Prothrombin Time (PT) Test Strip, High Control test strip and the Low Control test strip.

After visual inspection, a total of 30 PT test strips were functionally tested at designated time intervals, under varying storage conditions. 10 test strips were tested at each of three levels of Beckman Coulter Control Plasma. Measurements were conducted on the Immedia PT System and the ACL 100.

After visual inspection, 10 High Control and 10 Low Control test strips were functionally tested by adding 12 μ L of 15 mM calcium chloride to the test strip at designated time intervals, under varying storage conditions. Measurement of the PT in seconds was conducted on the Immedia PT System meter.

Stability Acceptance Criteria:

1. $CV \leq 5\%$.
2. Product visual appearance, pouch seals and packaging integrity maintained.
3. Change in percent difference from initial time "0" testing should be $\leq 15\%$ changed.
4. A condition must fail three consecutive time points to constitute a shelf life failure (using the same lot of lyophilized plasma controls).
5. Establishment of expiration date will be based upon real time testing and accelerated testing of test strips.

d. Detection limit:

Dilutions were prepared for each of four factor deficient plasmas (II, V, VII, X) by diluting with normal plasma to the following concentrations: 100%, 75%, 50%, 20%, 10%, 5%, 2.5% and 0% factor in the sample. Five replicates were tested of each

concentration of the prepared factors using the Immedia PT System. 12 μ L of each level was pipetted onto the test strip when prompted by the meter. The mean was calculated for each control test sample. The % factor in the sample versus the clotting time for each of the factors was plotted and the % factor depletion at which a change in the INR from normal is seen, thus identifying the sensitivity of the Immedia PT System for each factor.

The Immedia PT System is sensitive to factors II, V, VII, and X at the following levels: Factor II: 25%; Factor V: 50%; Factor VII: 50% and Factor X: 50%.

e. Analytical specificity:

Testing for interfering substances was performed according to CLSI guidance document EP7-A. Interfering substances tested include bilirubin, hemolysis, heparin, low molecular weight heparin and lipemia. For each interferent, different concentrations of the test pool and the control pool were tested on the Immedia PT System. Results were determined by calculating the difference between the mean of the test sample to the mean of the control sample.

Conclusion:

Bilirubin: <10% interference due to bilirubin of up to 20 mg/dL in the blood.

Hemolysis: <10% interference due to hemolysis of up to 500 mg/dL of hemoglobin concentration in the blood.

Heparin and Low Molecular Weight Heparin: Both cause significant interference in the therapeutic concentrations. Samples from patients undergoing with form of heparin therapy should not be tested on the Immedia coagulation system.

Lipemia: <10% interference due to triglycerides of up to 3000 mg/dL in the blood.

No evidence of interference was noted by the drugs listed in table of medications the sponsor provided.

The hemoglobin of each subject was tested using a HemoCue hemoglobinometer throughout the study. An estimate of hematocrit (3x Hgb) was plotted vs. the difference in INR between the Immedia PT System and the reference method results to determine the effect of hematocrit on the Immedia test results. No effect due to hematocrit was seen on the Immedia PT System over the measured INR range.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Accuracy - The method comparison study compared INR determinations obtained from the Immedia PT System and the predicate device (CoaguChek S) using capillary blood from a fingerstick compared to the WHO Standard method (gold standard). Results were compared with the INR result from the reference device (STA, using Innovin reagent).

Studies were conducted at three study sites (anticoagulation clinics). A minimum of 220 participants each providing a least one hanging drop from a fingerstick, and a 5 mL venous blood sample collected in 3.2% sodium citrate were tested. Test specimen summary: 20 normal volunteers, 155 any INR (< 3.0), and 45 with INR > 3.0 including 5 with an INR > 5.0.

Farallon Immedia PT System vs. CoaguChek S:

A single test result from each meter was used in the data comparison. The hanging drop was split between the two instruments, alternating the order of meters for each patient. A hematocrit level was performed from the same fingerstick at the point of care.

Laboratory Reference Method:

A 3.2% sodium citrate tube was drawn and centrifuged to create platelet poor plasma. It was then frozen and stored temporarily pending transfer to the reference laboratory. The reference laboratory tested all samples collected from the three sites in a single operation to minimize variables.

Patient inclusion/exclusion criteria:

- Patients not subject to any Farallon System limitations, including history of severe congenital or autoimmune hypofibrinogenemia, dysfibrinogenemia, hypoprothrombinemia, dysprothrombinemia, severe anemia, polycythemia or other blood dyscrasias
- Patient willing to have several fingersticks performed
- No contraindications to fingersticks or venous draws
- Subject 18 years of age or older
- Provide informed consent
- Patients not transitioning from heparin
- Patients on oral anticoagulation therapy (warfarin or other coumarin derivative)

Comparability was determined by evaluating the Farallon Immedia PT System capillary blood INR results versus results from the CoaguChek S System and the

WHO Standard. The data was analyzed separately and collectively for correlation slope and bias with regression analysis. Linear correlations for method comparison are listed below:

| Linear correlation (r value) | Immedia vs. STA | Immedia vs. STA excluding non-anticoag patients | Immedia vs. CoaguChek | Immedia vs. CoaguChek excluding non-anticag patients | CoaguChek vs. STA | CoaguChek vs. STA excluding non-anticag patients |
|------------------------------|-----------------|---|-----------------------|--|-------------------|--|
| PT | 0.92 | 0.89 | 0.90 | 0.85 | 0.93 | 0.90 |
| INR | 0.92 | 0.88 | 0.89 | 0.85 | 0.93 | 0.91 |

b. Matrix comparison:

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):

A single center method comparison study was conducted at Henderson Research Center (HRC), Hamilton, Ontario. Comparison testing was performed on the Immedia PT System and the CoaguCheck S. Calibration was determined by comparing PT results on the Immedia PT System with a lab reference device (STA, using Innovin) according to WHO Protocol for ISI determination and an international reference preparation, CRM 149S. Patient testing was completed within one hour and data from the three instruments were reported in both INR and PT seconds.

60 patients stabilized on warfarin or other coumarin derivative and 20 normal volunteers meeting the eligibility requirements were enrolled in the study. A minimum subset of 7 OAT patients with an INR ≥ 3.0 , as determined by the Immedia PT System, were required for the study. Each will provide two hanging drops, one from each of two fingersticks, and a 5 mL venous blood sample. The other 53 patients receiving OAT may represent any INR value.

Farallon Immedia PT System vs. CoaguChek S

Each patient had two fingersticks performed using different fingers by a trained member of the staff. The first hanging drop was drawn into a capillary tube, placed

into a micro vial and split between the Immedia PT System and the CoaguChek S device. The same process was repeated with the second hanging drop taken from a second fingerstick to yield two INR and PT results from each device for each patient.

Laboratory Reference Method

A 3.2% citrate anticoagulant tube was then drawn and centrifuged to create platelet poor plasma. It was then divided into three equal aliquots, 2 aliquots frozen and the third aliquot tested within 5 hours of collection, using the lab reference method and the WHO method.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

120 subjects healthy subjects not anticoagulated were tested based on CLSI Document C28-A. Testing was performed on the Immedia PT System using the same lot of test strips.

PT reference interval: 11.6 – 14.5 and INR range 0.8 – 1.2

N. Instrument Name:

Immedia Prothrombin Time System

O. System Descriptions:

1. Modes of Operation:

Table top single use device

2. Software:

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

Yes or No

3. Specimen Identification:

Barcode identification of the patient and control test strips.

4. Specimen Sampling and Handling:

Fresh capillary whole blood

5. Calibration:

The Immedia System is precalibrated. When the Calibration strip that comes in every Immedia test kit is inserted into the meter the bar coded calibration information is entered. Strips from different test kits or an expired strip will generate an error message and will not allow the test to be run.

6. Quality Control:

Liquid controls should be tested for each new lot number and/or shipment of test strips used. They may also be tested for trouble shooting purposes if unexpected results are obtained.

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

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.