CLIA Waiver by Application Approval Determination

Decision Summary

A. Document Number

CW230004

B. Parent Document Number

K230802

C. CLIA Waiver Type:

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

D. Applicant

Universal Biosensor Pty Ltd

E. Proprietary and Established Names

Xprecia Prime Coagulation System

F. Measurand (analyte)

Prothrombin Time (PT) reported in International Normalized Ratio (INR) and seconds

G. Sample Type(s)

Capillary whole blood from a fingerstick

H. Type of Test

Quantitative amperometric assay (detection of thrombin activity)

I. Test System Description

1. Overview

The Xprecia Prime Coagulation System has been designed to monitor INR and PT of patients undergoing anticoagulation therapy with warfarin (Vitamin K antagonist). It consists of the Xprecia Prime Coagulation Analyzer (meter) and Xprecia Prime PT/INR Strips.

The Xprecia Prime Coagulation System analyses a blood sample taken from the patient by fingerstick. The sample is transferred from the patient's finger to a test strip that has been inserted in the Xprecia Prime Coagulation analyzer. The blood is mixed with a reagent contained within the strip and the analyzer detects when clotting has occurred. The result is then displayed on the analyzer's screen in either units known as the International Normalized Ratio (INR) or in seconds.

2. Test System Components

   Xprecia Prime Coagulation Analyzer (Meter)
   Xprecia System PT/INR strips

3. Results Interpretation

   The Xprecia Prime Coagulation System provides a direct read-out of patient results at the completion of each sample analysis. Results can be displayed in either International Normalized Ratio (INR) or Prothrombin Time (PT) reported in seconds. To switch the units displayed, the user touches unit specifier beside the result. If an error occurs during testing, the result will not be displayed and instead an error code will be displayed on the screen.

J. Demonstrating "Simple"

- The Xprecia Prime Coagulation System consists of a fully automated Xprecia Prime Coagulation Analyzer and single use Xprecia Prime PT/INR test strips.
- The Xprecia Prime Coagulation System uses a direct unprocessed specimen - capillary whole blood (fingerstick). The sample requires no manipulation before performing the test.
- There is no reagent handling. Reagents are secured within the test strip. Once the test strip is inserted into the meter the sample is applied directly to the test strip and the test result is displayed. There are no further procedural steps.
- The Xprecia Prime Coagulation System provides direct readout of quantitative results that require no interpretation, or calculation by the operator.
- The Xprecia Prime Coagulation Analyzer does not require calibration or coding by the user. The detection of the calibration code is automatic by scanning the strip vial.
- The Xprecia Prime Coagulation System requires no operator intervention during the analysis steps.
- The Xprecia Prime Coagulation System requires no technical or specialized training with respect to troubleshooting or interpretation of multiple or complex error codes. Error messages are unambiguous and include easy-to-interpret solutions.
- The Xprecia Prime Coagulation System requires no electronic or mechanical maintenance. Maintenance of the meter consists of general external cleaning, disinfection, and plugging the meter in to charge.
- The Xprecia Prime Coagulation System labeling (Quick Start Guides (QSGs) and User Guide) are simple and QSGs are written at a 7th grade comprehension level.

K. Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-safe Mechanisms

1. Risk Analysis

Following the two-tiered approach recommended in the FDA's *Guidance for Industry and FDA staff: Recommendations for Clinical Laboratory Improvement Amendments (CLIA) of 1988 Waiver Application for Manufacturers of In Vitro Diagnostics Devices*, a comprehensive risk analysis was conducted for the Xprecia Prime Coagulation System as a part of risk management process to demonstrate that the device is robust and has appropriate and effective risk control measures. All risks of harm to the patient or operator were mitigated to an acceptable level and were supported by flex studies and/or operator instructions.

2. Fail-Safe and Failure Alert Mechanisms

a. Warning and Error Messages

Warnings inform the user there is something that needs to be corrected before a process can continue. The following warnings can be displayed by the meter:

Warning Code	Cause	Users should do
20-01 Bad barcode	A barcode was scanned but could not be read. This could either be because the barcode is damaged or not in a recognized format.	Check that the barcode isn't damaged. Ensure that all parts of the barcode are visible and not obscured during the scan. Try wiping the barcode clean and trying again.
20-02 Remove strip	The test strip was inserted at an inappropriate time. The test strip should only be inserted after the analyzer displays the Insert strip screen.	Discard the strip and start a new test. The strip must not be reused after it has been inserted into the strip port.
20-03 Wrong vial	The barcode on the test strip does not match the barcode on the vial. Test strips are coded to match the vial from which they came from.	When prompted to scan a vial barcode, always be sure to scan the vial from which the strip was taken.
20-04 Strip not valid	The analyzer tried to scan a strip barcode, but the barcode is not from an Xprecia Prime PT/INR Test Strip.	When prompted to scan a strip, always scan an Xprecia Prime PT/INR Test Strips. You must only use Xprecia Prime PT/INR Test Strips. Other strips (e.g. PT/INR Strips for other Xprecia Systems) – will not work with the Xprecia Prime analyzer.
20-05 Fit the End Cap	The strip port's protective end cap (see item 4 on page 12) is not correctly fitted.	Fit the protective cap to the strip port. Keep the strip port's protective end cap firmly fitted at all times (except during cleaning – see page 45).
20-06 LQC strip mismatch	The analyzer read a barcode, but the scanned strip barcode is not compatible with the scanned LQC barcode.	You must only use Xprecia Systems PT Controls and Xprecia Prime PT/INR Test Strips. Other strips (e.g. PT/INR

Warning Code	Cause	Users should do
		Strips for other Xprecia Systems) – will not work with the Xprecia Prime analyzer.
20-07 Invalid Patient ID	The administrator has set length limits for the Patient ID. The scanned or entered Patient ID is too short or too long.	Check that you have scanned or entered a valid Patient ID. See your administrator if the problem persists.
20-08 Invalid Operator ID	You have tried to log in with an Operator ID that is not recognized.	Check that you have scanned or entered a valid Operator ID. See your administrator if the problem persists.
20-09 Invalid strip barcode	The analyzer tried to scan a strip barcode, but the barcode that was scanned was not valid. The analyzer tried to scan a strip barcode, but there are problems with the information in the barcode, and it did not pass the quality check. There might be issues with the barcode readability.	When prompted to scan a strip, always scan an Xprecia Prime PT/INR Test Strips. Discard the test strip and start the test again with a new strip. If the error persists, contact Customer Support (see page 90).
20-10 Invalid vial barcode	The analyzer read a barcode, but the scanned barcode is not from an Xprecia Prime PT/INR Test Strip vial.	When prompted to scan a strip vial, always scan an Xprecia Prime PT/INR Test Strips vial. You must only use Xprecia Prime PT/INR Test Strips. Other strips (e.g. PT/INR Strips for other Xprecia Systems) – will not work with the Xprecia Prime analyzer.
20-11 Invalid LQC barcode	The analyzer tried to scan a LQC barcode, but there are problems with the information in the barcode, and it not pass the quality check. There might be issues with the barcode readability.	When prompted to scan a strip vial, always scan a Xprecia™ Systems PT Controls bottle. You must only use Xprecia Systems PT Controls. All other LQC kits will not work.
20-13 LQC test due	The analyzer is set to lockout if a LQC test is not performed periodically. In the near future, a lockout will occur unless the required LQC test(s) is performed successfully.	You can still run patient tests at this time, but an LQC test should be performed soon. See your administrator for details.
20-15 Battery critical	The battery level has become critical (less than 20%) while a test is in progress. If a test has already been started prior to this warning message appearing, the test can be completed.	Before a new test can be started you must connect the analyzer to an external power source, which will also charge the battery.

Warning Code	Cause	Users should do
20-16 Battery critical	The battery level has become critical and there is insufficient battery to perform a test	Before a new test can be started you must connect the analyzer to an external power source, which will also charge the battery.
20-20 Battery Critical	The battery level has become critical and the device will shut down unless connected to power immediately	You must connect the analyzer to an external power source, which will also charge the battery.
20-21 Power not connected	When a software update is being performed the analyzer must be connected to external power. This is to ensure that the update will not be interrupted.	Connect the analyzer to external power and start the software update again.
20-22 Software update failed	Something stopped the software update from being performed.	Start the software update again. If it continues to fail, contact Customer Support (see page 90). In the meantime, you can continue to use your analyzer using the existing software version.
20-24 LQC test is due	The analyzer is locked out because a LQC test was not performed at the time set by your administrator.	If the patient test is urgent, you can choose to bypass the LQC lockout. See your administrator for details.
20-24 Bad password	You have tried to log in with a password that is not valid for the given Operator ID.	Check that you have scanned or entered the right password. See your administrator if the problem persists.
20-26 Operator List Empty	The analyzer has been configured to require Operator login, but the Operator List is empty	Follow the instructions on page 70 to set up an operator list on the analyzer.

Errors inform the user of an issue that is not recoverable (e.g., an issue that requires the test to be restarted with a new strip). The following error messages can be displayed by the meter:

Error Code	Cause	Users should do
40-01 Below minimum range	The measured result was below the measuring range of Xprecia Prime (less than 0.8 INR).	Repeat the test with a fresh sample. Such results should be confirmed using an alternative test method (e.g. laboratory PT/INR).
40-02 Above maximum range	The measured result was above the measuring range of Xprecia Prime (greater than 8.0 INR).	Repeat the test with a fresh sample. Such results should be confirmed using an alternative test method (e.g. laboratory

Error Code	Cause	Users should do
		PT/INR).
40-04 Below LQC minimum	The LQC test failed because the result was below the expected range. There are a number of possible causes for this. See Page 76 for guidance.	Perform the troubleshooting steps on Page 76.
40-05 Above LQC maximum	The LQC test failed because the result was above the expected range. There are a number of possible causes for this. See Page 76 for guidance.	Perform the troubleshooting steps on Page 76.
50-02 Test timeout	Test time out. An analysis error occurred and the test result could not be calculated. Possible causes include too much analyzer movement, an unsupported sample type, a system fault, or test strips that have not been stored correctly.	Discard the test strip and start the test again. Apply the sample as instructed on page 31. If the error persists, contact Customer Support (see page 90).
50-03 OBC failure	The test strip's on-board control (OBC) has detected that the strip is damaged and cannot be used. Possible causes include test strips that are damaged or test strips that have not been maintained properly.	Discard the strip and start a test with a new strip from the same vial (if available). If the error persists and you are sure the vial has been kept closed and at the correct storage temperature (see Page 95), contact Customer Support (see page 90).
50-04 Partial fill	Insufficient sample was applied to the strip and the test could not be completed.	You must not apply additional sample to the test strip after the test has begun. Discard the strip and start the test again. Apply the sample as instructed on page 31.
50-05 Double fill	Two or more sample dose applications were detected during application and the test could not be completed	You must not apply additional sample to the test strip after the test has begun. Discard the strip and start the test again. Apply the sample as instructed on page 31.
50-08 Pre double fill	Two or more sample dose applications were detected during application and the test could not be completed.	You must not apply additional sample to the test strip after the test has begun. Discard the strip and start the test again. Apply the sample as instructed on page 31.
50-09 Uneven fill	The sample could not reach the strip's reaction chamber correctly. Possible causes include too much	Discard the test strip and start the test again. Apply the sample as instructed on page 31 . If the

Error Code	Cause	Users should do
	analyzer movement, an unsupported sample type or a system fault.	error persists, contact Customer Support (see page 90).
70-10 User abort	The user aborted a test after the strip was inserted.	Discard the strip and start a new test. The strip must not be reused after it has been inserted into the strip port.
70-11 Insert strip timeout	The strip was not inserted within the time limit on the Insert strip screen.	Start the test again and insert the strip when prompted by the analyzer.
70-12 Temperature error	The analyzer could not adequately control the strip's temperature.	Make sure the ambient temperature is between 15°C and 32 °C (59 °F to 89 °F) and restart the test with a new strip. You may need to allow time for the analyzer's temperature to stabilize. If the problem persists, contact Customer Support (see page 90).
70-13 Used strip	The inserted strip has already been used for a test (or the strip might have been handled with wet hands).	Discard the strip before starting a new test. If the error recurs, try a new vial of strips.
70-14 Early sample	The sample was applied too early.	Discard the strip before starting a new test. Apply the sample only when prompted by the analyzer.
70-15 Strip removed early	The test strip was removed before the test was finished.	Discard the strip before starting a new test. Ensure the strip is pushed fully into the strip port, and don't remove the strip until instructed.
70-16 Expired test strip	The test strip is past its expiry date.	Start the test again with a new strip from a vial that has not expired.
70-18 Internal Error	The graphical user interface was forced to reset due to an error.	Turn the analyzer off and on. If the same error occurs, contact Customer Support (see page 90).
70-19 Internal Error	The graphical user interface generated an error.	Turn the analyzer off and on. If the same error occurs, contact Customer Support (see page 90).
70-20 End cap removed	During a test, the strip port's protective end cap (see item 4 on page 12) was removed.	Fit the protective cap to the strip port and restart the test with a new test strip. Keep the strip port's protective end cap firmly fitted at all times (except during cleaning) (see page 45).

Error Code	Cause	Users should do
70-21 Sample not applied	The sample was not applied at the time requested by the analyzer.	Discard the strip before starting a new test. Apply the sample when prompted by the analyzer.
70-23 LQC lockout	Your analyzer is set to lockout when either a LQC test fails or a LQC test is not performed periodically. A patient test cannot be performed until the required LQC test(s) is performed successfully.	Run a passing LQC test (or LQC tests if your analyzer requires Level 1 and Level 2 LQC to be performed). See your administrator for details.
70-24 Battery critical	The battery is too low to start a new test.	Before a new test can be started you must connect the analyzer to an external power source, which will also charge the battery.
70-25 LQC Expired	The LQC kit is past its expiry date.	Start the test again with a new LQC kit that has not expired.
70-26 Invalid transient	An issue with the collected test result was identified and the test result could not be obtained.	Turn the analyzer off and on. If the same error occurs, contact Customer Support (see page 90).
80-00 Internal error	There was an internal error, and the test result could not be read from the result log.	Turn the analyzer off and on. If the same error occurs, contact Customer Support (see page 90).
16-XXXX Self test timeout	The analyzer has not passed it's internal self test checks. Note: XXXX is a diagnostic number and will differ depending on the cause of the self test error.	Turn the analyzer off and on. If the same error occurs, contact Customer Support (see page 90).
17-0000 Battery too low	The battery is too low for the analyzer to operate, most likely because the analyzer has not been used for a very long time.	Before the analyzer can be used, you must connect the analyzer to an external power source to charge the battery enough for it to be used safely. This may take 30 minutes or more.
20-000 Software Verification Error	The analyzer software has not passed its self verification checks and there may be an issue with the analyzer software.	Turn the analyzer off and on. If the same error occurs, reinstall the analyzer software or contact Customer Support or (see page 90).

b. External Control Materials:

The User Guide and QSGs state to only use the Xprecia Systems PT Controls (Liquid quality control (LQC) solution Level 1 and 2; K151964) with the Xprecia Prime Coagulation System. External controls should be performed with every new lot, new shipment, or as required by local, state, and federal or national regulations. New operators should perform LQC prior to

starting to perform patient testing. Use of external QC ensures that the Xprecia Prime Coagulation System is working as designed.

Each Xprecia Systems PT Controls kit contains two levels of vials of plasma and diluent. The reconstitution of the LQC requires the user to pipette the diluent solution into the plasma vial and let the solution stand for at least 5 minutes. The INR target of the reconstituted LQC 1 will be around 1.0 INR and LQC 2 will be in the therapeutic range of oral anticoagulant therapy, INR of 2.0–4.5. The User Guide and the QRG for Liquid Quality Control provide basic instructions for testing the meter with the control material.

Directions for use are clearly stated in the labeling (QSG and User Guide). Storage and stability are stated in the User Guide. The user should follow the manufacturer's instructions for storage and stability.

3. Flex Studies

Based on risk analysis and the identification of potential errors, the following flex studies were conducted on the Xprecia Prime Coagulation System to demonstrate that the test system is robust when its operational limits are stressed due to potential operator errors, factors affecting specimen or test system integrity, or environmental factors. The studies were conducted using the Xprecia Prime Coagulation Analyzer and Xprecia Prime PT/INR Test Strips:

System Operating Conditions Testing:
To assess the performance of the Xprecia Prime Coagulation System when used under various operating temperature and humidity conditions, the system was tested at four different temperature and humidity conditions including low temperature/low humidity (10°C/ 7% RH), low temperature/high humidity (14 °C/ 90% RH), high temperature/low humidity (35°C/ 5% RH) and high temperature/high humidity (36°C/ 90% RH). Each of 3 whole blood samples (normal, INR 2.0–4.5 and INR 4.0–8.0) and LQC Level 1 and 2 were tested by 3 analyzers, using 3 lots of test strips, for a total of 16 replicates at each operating condition and sample. For each operating condition and each sample, the mean INR was calculated across all strip lots. The percent bias was calculated using the mean INR compared to the appropriate control sample mean result at ambient conditions (22°C/ 40% RH). The results of the study demonstrate that accurate test results can be obtained when the system is operated at the specified operating conditions of 15–32°C and 10–85% RH.

PT/INR Test Strip – Reagent Quality Control Testing
A flex study was performed to evaluate the software fail-safe mechanism for the validation of the presence of the required strip reagents. In this study, Xprecia Systems PT Controls LQC 1 and LQC2 and whole blood from normal donors and warfarin donors were used for testing in replicates of eight on 24 analyzers using three strip lots. There were 32 tests conducted on each strip type – strips without thromboplastin reagent, strips without substrate reagent, and strips without both reagents. All three strip conditions (without thromboplastin, without substrate, and without both reagents) resulted in an error 100% of the time as expected.

PT/INR Test Strip – Operating Conditions Testing
A flex study was performed to evaluate the software fail-safe mechanism for the verification of strips that have been affected by exposure environmental conditions outside of the claimed stability. Xprecia Prime PT/INR Test Strips have a claimed out-of-vial stability of 10 minutes

at 2–30°C at <75% RH. In this study, whole blood from normal donors and warfarin donors were used for testing in replicates of eight on 24 meters using three strip lots. One set of strips was used as the control set and was removed from the vial tested within 10 minutes at claimed storage conditions of 2–30°C at <75% RH. All other strips were removed from the vial and exposed to environmental conditions of 30°C and >75% RH for 10, 20, 30, 40, and 50 minutes. The results of the study demonstrate that accurate test results can be obtained when strips are used at the claimed operating conditions of 2–30°C at <75% RH and within 10 minutes from vial removal. The meter has an error message displayed if the strips were exposed beyond 10 minutes and at subsequent times of 20, 30, 40, and 50 minutes. This feature was validated and was shown to function as intended.

Re-used Strip

A flex study was performed to evaluate the software fail-safe mechanism for re-used strips on the meter. Strips pre-filled with whole blood from normal donors, warfarin donors or LQC 1 or 2 were inserted into 24 different meters to test if the software can detect an already used strip and produce a used strip error. The meter displayed an error message for each tested sample type. This feature was validated and was shown to function as intended.

Incorrect Strip Orientation

A flex study was performed to evaluate the software fail-safe mechanism to detect the correct strip orientation into the meter. Strips were inserted into the 24 different meters in different orientation other than the correct one. These 3 incorrect orientations are upside down, porch first and upside down with the porch first. The System is unable to produce a result as tests were not able to start due to the strips not detected by the Analyzer. Each meter stayed on the "insert strip" screen. This feature was validated and was shown to function as intended.

Minimum Volume Study:

A flex study was performed to evaluate the software fail-safe mechanism to detect a partially filled strip. The minimum sample volume for the Xprecia Prime System is 8.0 µL. The study tested whole blood from normal and warfarin donors and LQC 1 and 2 at 4.0, 4.5, 5.0, 5.5, 6.0, and 8.0 µL volumes in 3 replicates using 3 strip lots across 24 different meters. For samples under 6.0 µL the meter displayed an error message for each tested sample volume tested. Measurements on samples tested at 6µl still produces comparable results to 8 µL samples, but the minimum sample volume is claimed as 8 µL more conservatively to maximize user comfort and ease in sample application. The partial fill error feature was validated and was shown to function as intended.

An additional study was performed which tested whole blood from normal and warfarin donors and LQC 1 and LQC 2. Eight replicates per 3 unique strip lot was performed for each run tested. Each test run consists of four analyzers immediately after sample collection and four analyzers 60 seconds later, will give a total of 24 replicates for the three lots in combination (2-time durations x 4 analyzer/per time duration x 3 strip lots = 24 analyzer/sample type). Samples were tested at 8.0 and 12.0 µL volumes. For each test sample and each strip lot, the average INR values at 8.0 µL sample application volume are compared to the INR result at a 12.0 µL sample application volume. The results of the study support a claimed minimum sample volume of 8 µL.

Uneven Fill Error

A flex study was performed to evaluate the software fail-safe mechanism to detect when the

strip is not filled evenly. The sample should fill the entire sample application area on the test strip. The study tested whole blood from normal and warfarin donors and LQC 1 and 2 in 3 replicates using 3 strip lots across 24 different meters. Samples were added to the test strip application area in an uneven orientation to not fill the entire sample area. If sample does not fill the test strip application area evenly, the meter displays an error message. For all samples applied unevenly the meter displayed an error message for each tested sample type. This feature was validated and was shown to function as intended.

Double Fill Errors

A flex study was performed to evaluate the software fail-safe mechanism to detect when an operator double fills the strip with either patient sample or LQC material after the test strip has been completely filled and the device is processing and analyzing the sample. This study tested whole blood from normal and warfarin donors and LQC 1 and 2 in 3 replicates using 3 strip lots across 24 different meters. Testing was performed 1.5–3.0 seconds, 3.0–5.3 seconds, and > 5.3 seconds after the meter indicated it was analyzing the sample. The device is designed to display an error message is sample is applied 1.5–3.0 seconds (Pre-Double Fill Low error), 3.0–5.3 seconds (Double Fill Low error), and > 5.3 seconds (Double Fill) after device is analyzing on the screen. The results of the study demonstrated the device displays an error message when a sample is added to the test strip after the device is analyzing at 1.5–3.0 seconds (Pre-Double Fill Low error), 3.0–5.3 seconds (Double Fill Low error), and > 5.3 seconds (Double Fill error). The feature is validated and was shown to function as intended.

Sample Added Early Error

A flex study was performed to evaluate the software fail-safe mechanism to detect when an operator adds the sample to the test strip prior to the meter being ready. After inserting a test strip into the meter, the screen displays a preparing message and indicates to the user to not apply sample yet. When the meter is finished preparing, the screen will display a 'Apply sample now' message with a 5-minute timer. This study tested whole blood from normal and warfarin donors and LQC 1 and 2 in 3 replicates using 3 strip lots and 24 different meters. The time limit for test strip preparing can vary due to different factors (e.g., temperature readings, strip integrity measurements, etc.), therefore the study added the sample as soon as the strip was placed into the meter and the 'preparing' message was displayed < 3 seconds. The results of the study indicated all samples applied early yielded an error message. This feature is validated and was shown to function as intended.

Strip Removed Early Error

A flex study was performed to evaluate the software fail-safe mechanism to detect when an operator removes the strip too early from the meter. When a sample is being analyzed, the meter displays it is Analyzing on the screen. The QSG states to wait for the analysis to complete before performing any additional actions and the strip is to be ejected after the result screen is displayed. This study tested whole blood from normal and warfarin donors and LQC 1 and 2 in 3 replicates on strip lots and 24 different meters. To test the feature, all test strips were removed during the Analyzing phase. The results of the study indicated all test strips removed too early (during analysis) yielded an error message. This feature is validated and was shown to function as intended.

Outside Measuring Range

A flex study was performed to evaluate the software fail-safe mechanism to detect when a result is outside of the meters measuring range (< 0.8 or > 8.0) or the LQC is outside of the

expected LQC range. The meter will display an error message if the results is < 0.8 and > 8.0 INR for patient samples and if the LQC is outside of the expected range. This study tested whole blood from normal and warfarin donors and LQC 1 and 2 in replicates of 3 on 3 different strip lots and 24 different meters. The results of the study indicated patient samples outside of 0.8–8.0 INR yield an error message and LQC material outside of the expected LQC range yield an error message. This feature is validated and was shown to function as intended.

Vibration Testing

A flex study was performed to evaluate the effect of vibration on whole blood from normal and warfarin donors and LQC 1 and 2 on the Xprecia Prime Coagulation Analyzer. The analyzer was subjected to three levels of vibration: 4.8 mm/s, 10 mm/s, and 15 mm/s and at two frequencies: 51.7Hz and 66.7Hz. Samples were tested in duplicate at each vibration level and frequency. Results were compared to the same sample levels tested without vibration. The results demonstrate the expected vibration condition at the waived sites does not affect the performance of the Xprecia Prime Coagulation System.

Drop Testing

A flex study was performed to assess the Xprecia Prime Coagulation Analyzer's ability to withstand rough handling over the products design life with the tests conforming to IEC 61010-1 - shock (drop). Three Xprecia Prime Coagulation Analyzer were dropped from a height of 1 m (3.3 ft), from each of the analyzer's six sides. No hazards were identified from the visual inspection. All three analyzers remained functional, and LQC 1 and 2 test results reported by the analyzers were within the LQC expected range with no erroneous LQC results produced. The Xprecia Prime Coagulation System can withstand rough handling.

Analyzer Orientation Study – Pitch and Roll

A flex study was performed to assess the Xprecia Prime Coagulation System's ability to monitor its angle in roll and pitch during the apply sample and analysis steps and report an error if the angle is greater than ±90 º. This study tested whole blood from normal and warfarin donors and LQC 1 and 2 in replicates of 8 on 1 strip lot and 1 analyzer. The analyzer performed testing on a flat surface with 0° degree of angle and at angles of 65° and 90° degree (pitch) ± 2 ° in positive and negative directions from the horizontal plane and in "roll" orientation in opposite directions. The results of the study indicated the analyzer can produce results for both patient and LQC samples at 65° and 90° (pitch) angles comparable to 0° degree of angle results. The device performance is acceptable at 0°, 65°, and 90° (pitch) angles.

Test Strip Storage Stability

A real-time shelf-life stability study was conducted using 3 lots of test strip lots at 5ºC with ambient RH (40± 20%) and 30ºC with 75% RH storage conditions. Three levels of quality control material (K151964–Xprecia System PT Control Level 1 and 2 and K771346–Ci-Trol Coagulation Control III), unaltered whole blood samples to reflect normal INR range and warfarin treated samples to reflect therapeutic INR range were tested at time zero and ten different test events: 4.5, 6, 7, 9, 12, 15, 18, 21, 24, and 27 months. The stability results for the Xprecia Prime PT/INR Strip lots support a shelf-life of 24 months at 5ºC–30ºC with < 75% RH.

Robustness Study:

Disinfection efficacy studies were performed on the exterior meter materials by an outside

commercial testing laboratory, demonstrating complete inactivation of Hepatitis B Virus (HBV) with the chosen disinfectant, Caviwipe™. Robustness studies were also performed by the sponsor demonstrating that there was no change in performance or external materials of the meter after 8,961 cycles of cleaning and disinfection using the chosen disinfectant. The robustness studies were designed to simulate cleaning and disinfection over the 3-year multi-patient use life. The validated cleaning and disinfection instructions are included in the labeling.

Electromagnetic Interference

The sponsor provided documentation certifying that acceptable electrical safety and electromagnetic compatibility (EMC) testing had been performed and the system was found to be compliant.

L. Demonstrating "Insignificant Risk of an Erroneous Result"

1. Comparison Study

a. *Study Design*

i. Study Sites

Method comparison studies were conducted at four U.S. point-of-care clinical sites with at least CLIA certificates of Waiver. The sites consisted of primary care clinics, coagulation clinics, and family practice offices. All the sites qualified as representative of CLIA waived intended use sites for the Xprecia Prime Coagulation System.

ii. Operators

In total, 11 operators participated in the clinical study of the Xprecia Prime Coagulation System. The operators selected for the study were representative of operators in a CLIA waived setting and were untrained in the use of the Xprecia Prime System (non-laboratory personnel, e.g., medical assistants, administrative personal, research coordinators, and phlebotomists). The operators had no previous experience participating in PT/INR coagulation meter testing.

iii. Instructions for Use

The operators were given the meter, test strips, control solutions, the User Guide, and both QSGs in order to self-train. Operators used the User Guide and both QSGs to self-train to conduct a control test, conduct a patient test, view past results, and understand the cleaning/disinfection procedure and recommendations. No other materials or instructions were provided, and the operators received no training on the use of the system.

iv. Subjects (Patients)

A total of 450 subjects, 18 years of age and older were enrolled into two groups. Group 1 consisted of 320 patients on warfarin therapy for at least six weeks prior to enrollment and Group 2 consisted of 130 healthy, normal patients. No contrived or altered samples were

tested in the clinical study.

Exclusion criteria:

- Skin lesions or conditions that would preclude fingerstick blood collections.
- The subject is currently taking any other anticoagulants (including but not limited to apixaban, dabigatran, edoxaban, rivaroxaban) NOTE: This exclusion does not include subjects on antiplatelet therapies such as aspirin (<325mg/day).
- Currently receiving or has received within the past thirty (30) days of the study visit an experimental biologic, drug or device, including either treatment or therapy.

v. Samples

A patient's participation in this study consisted of a single visit. Each patient had two fingerstick samples collected by the untrained operator for testing on the Xprecia Prime Coagulation System and the comparator, CoaguChek XS (K060978).

vi. Comparative Method (CM)

Roche CoaguChek XS (K060978)

b. *Results and Analysis*

i. Allowable Total Error (ATE) Analysis

The results from the capillary fingerstick whole blood samples obtained from the Xprecia Prime System Coagulation System (Candidate) were compared to the results from the comparator method (CoaguChek XS). Data were analyzed for each site separately and for all sites combined. The data for all combined data are summarized below:

Comparison of the Xprecia Prime Coagulation System INR results vs CoaguChek XS INR

Subinterval by Comparator	ATE	N	Percent of samples with ATE (95% CI)
0.8–1.9	±20%	170	98.2% (166/167) (94.9%; 99.4%)
2.0–3.5	±20%	140	95.0% (133/140) (90.0%; 97.6%)
3.6–4.5	±20%	67	94.0% (63/67) (85.6%; 97.7%)
4.6–8.0	±25%	64	95.3% (61/64) (87.1%; 98.4%)
Combined 0.8–8.0		438	96.1% (421/438) (93.9%; 97.6%)

For combined data, the percent of samples within the ATE was 96.1% (421/438) with 95% CI: (93.9%; 97.6%).

Comparison of the Xprecia Prime Coagulation System PT results vs CoaguChek XS PT

Subinterval by Comparator	ATE	N	Percent of samples within ATE (95% CI)
10.6–24.2	±20%	193	97.9% (189/193) (94.8%; 99.2%)
24.3–56.8	±20%	197	96.4% (190/197) (92.8%; 98.3%)
≥56.9	±25%	48	89.6% (43/48) (77.8%; 95.5%)
Combined		438	96.3%. (422/438) (94.1%; 97.7%)

For combined data, the percent of samples within ATE was ATE was 96.3%. (422/438) with 95% CI (94.1%; 97.7%).

ii. Limits for Erroneous Results (LER) Analysis

The clinical study found no INR values within the LER zones:

a) X is <2 and Y is >3 and

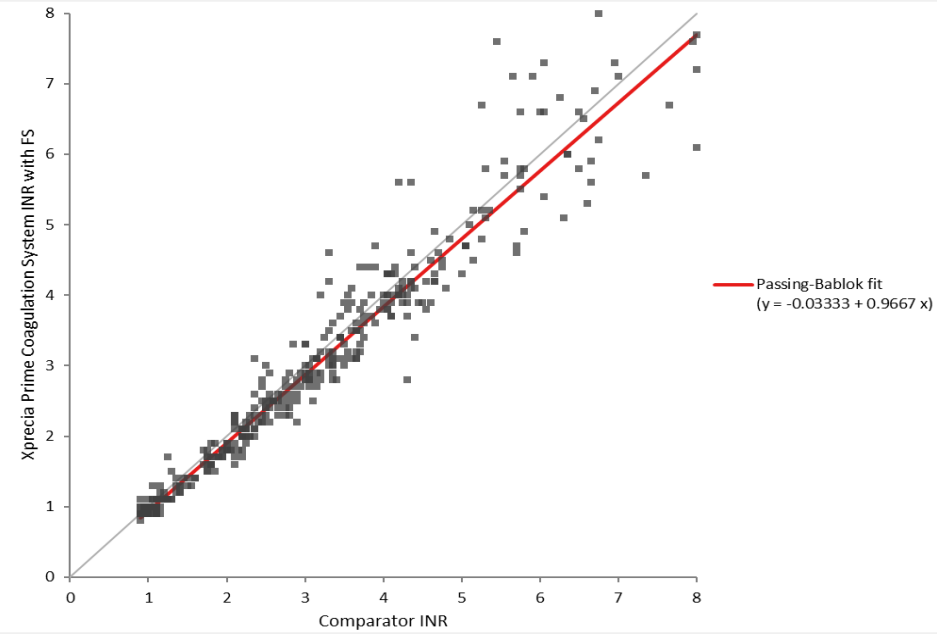
b) X is >3 and Y is <2

where X is a value of the Comparator and Y is the value of the Candidate.

Percent of samples in the LER zone was 0.0% (0/435) with 95%CI: (0.0%, 0.9%).

iii. Regression Analysis for Estimation of %Biases

For the estimation of %Biases, it was performed Passing-Bablok regression analysis. The results of the regression analysis were: slope=0.967 with 95%CI: (0.947; 0.985) and intercept=-0.033 with 95%CI: (-0.080; -0.002). Scatter plot and the regression line is presented below:



Biases and %Biases were calculated and presented in the table below.

X*, Comparator INR	Bias	%Bias	95%CI for %Bias
1.0	-0.07	-6.7%	(-9.8%; -4.8%)
2.0	-0.10	-5.0%	(-6.6%; -4.2%)
3.0	-0.13	-4.4%	(-5.9%; -3.6%)
4.0	-0.17	-4.2%	(-5.6%; -3.1%)
6.0	-0.23	-3.9%	(-5.4%; -2.6%)

2. Operator Questionnaire

Upon completion of the clinical studies, each of the 11 operators completed a questionnaire. The participants found Xprecia Prime System easy to use and the instructions in the User Guide and QSGs clear and easy to follow.

M. Labeling for Waived Devices

The labeling consists of:

1. Quick Start Guide – Patient Test
2. Quick Start Guide – Quality Control Test
3. User Guide
4. Xprecia Prime PT/INR Strip Package Insert
5. Meter Carton
6. Test Strips Carton

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

- The Quick Start Guides (QSG) and User Guide are written at no higher than a 7th grade reading level.
- The User Guide and QSG identify the test as CLIA waived.

- The User Guide and test cartridge package insert contain a statement that a Certificate of Waiver is required to perform the test in a waived setting.
- The User Guide and QSG contain a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test. 42 CFR 493.15(e)(1).
- The User Guide and QSG provide instructions for conducting quality control procedures.

N. Conclusion:

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.