CLIA Waiver by Application Approval Determination

Decision Summary

A. Document Number

CW250013

B. Parent Document Number

K252323

C. CLIA Waiver Type:

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

D. Applicant

Roche Diagnostics

E. Proprietary and Established Names

cobas® pulse blood glucose monitoring system

F. Measurand (analyte)

Glucose

G. Sample Type(s)

Arterial whole blood, neonatal arterial whole blood, neonatal heel stick whole blood, and venous whole blood anticoagulated with lithium heparin.

H. Type of Test

Quantitative amperometric assay (FAD-dependent glucose dehydrogenase)

I. Test System Description

The cobas® pulse glucose monitoring system consists of a hand-held, battery powered cobas® pulse instrument, instrument charging station, and single use cobas® GLU test strips. The GLU QC kit is sold separately. The system utilizes amperometric detection as the test principle utilizing FAD-dependent glucose dehydrogenase (FAD-GDH) for the quantitative determination of glucose concentrations in arterial, neonatal arterial, neonatal heel stick and venous whole blood samples. Glucose in the blood reacts with the reagent in the test strip, and this produces a small electric current (amperometry). The magnitude of the resultant current is proportional to the glucose concentration in the sample. The detected current signal is then calculated by the meter and the glucose concentration is displayed on the meter. The meter reports plasma equivalent glucose concentrations.

J. Demonstrating "Simple"

- The cobas pulse blood glucose monitoring system consists of the fully automated cobas pulse instrument and single-use cobas GLU test strips.

- The cobas pulse blood glucose monitoring system uses direct, unprocessed whole blood samples and requires no sample manipulation before performing the test.

- There is no reagent handling. Reagents are secured within the test strip. The meter provides the user with step-by-step prompts on the touch screen describing how to run a glucose test. 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 cobas pulse blood glucose monitoring system provides direct readout of quantitative results that require no interpretation, or calculation by the operator. No operator intervention is required during the analysis steps.

- The cobas pulse blood glucose monitoring system does not require calibration or coding by the user. The cobas® pulse instrument is factory calibrated.

- The cobas pulse blood glucose monitoring 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 cobas pulse blood glucose monitoring system requires no electronic or mechanical maintenance. Maintenance consists of charging the meter using the provided charging station, and external cleaning and disinfection of the instrument.

- The cobas pulse blood glucose monitoring system includes a quick reference guide (QRG) and instructions for the CLIA waived user in the user guide are written at no higher than a 7th grade comprehension level.

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

1. Risk Analysis

A comprehensive risk analysis was conducted by the sponsor for the cobas pulse system to assess the risks of providing incorrect patient results and the safety risks to the patient or operator associated with the operation of the system and to demonstrate that the system is robust to known sources of error. All risks of harm to the patient or operator were mitigated to an acceptable level, and the system was demonstrated to be robust to known sources of error.

2. Fail-safe and Failure Alert Mechanisms

a. Error Messages and Lock-outs:

The cobas pulse system was designed with several failure alert mechanisms and procedural controls intended to reduce the risk of device malfunction and procedural errors when performing the assay. The system will provide an error message, or a lockout function will occur and will not allow output of test results. For example:

- **B-AA**: Invalid barcode. If the barcode is invalid, the error message will be displayed, and the user is advised to try again and if the problem persists to contact their system administrator or Roche customer support if they do not have a system administrator onsite.
- **B-AB**: Scanning timeout. If the barcode scanning period has timed out, the error message is displayed, and the user is advised to prepare the barcode and restart scanning the barcode.
- **D-AA**: Test strip error. If there is a test strip error due to wrong position of the test strip, damaged test strip or dirty test strip, the error message will be displayed and the user is advised to repeat the test with a new test strip.
- **D-AB**: Lot expired. If the test strip lot has expired, the error message will be displayed, and the user is advised to repeat the test with a test strip from an unexpired lot.
- **D-AE:** Material expired. If the QC material is expired, the error message will be displayed, and the user is advised to use to check expiry date and repeat the tests with a new test strip and a QC material that is not expired. If the problem persists, the user is instructed to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite.
- **D-AF:** Test strip error. If there is a test strip error due to an already used strip or test strip container left open, the error message will be displayed, and the user is advised to repeat the test with a new test strip and to contact system administrator or they can contact the Roche customer support if they do not have a system administrator onsite
- **D-AG:** Insertion error. If the test strip is not inserted completely, the error message will be displayed, and the user is advised to eject the test strip and insert

it again ensuring that it is fully pushed inside the instrument. If the problem persists, the user is instructed to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite.

- **D-AH:** Unknown lot. If the instrument does not recognize the test strip lot, the error message will be displayed, and the user is advised to ensure that a correct test strip lot is used and try again. If the problem persists, the user is instructed to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite.
- **D-AJ:** QC test required. If QC testing is required to be performed, the error message will be displayed, and the user is advised to perform a QC test.
- **D-AK:** Insertion error. If the test strip is inserted too early, the error will be displayed, and the user is advised to eject the test strip and to wait for the screen instruction before inserting the test strip.
- **D-AL:** Test strip error. If the test strip was removed during testing, the error message will be displayed, and the user is advised to repeat the test with a new test strip and warned to not remove the test strip during processing. The user is advised to always use the eject button to remove the test strip.
- **D-AN:** Unknown kit lot. If an unknown QC kit lot is used, the error message will be displayed, and the user is advised to ensure that a correct QC kit lot is used and to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite.
- **D-AO:** Test strip error. If the eject button was not used to remove the test strip, the error message will be displayed, and the user is advised to use the eject button to remove the test strip and to repeat the test with a new test strip.
- **E-AA:** Temperature too low. If the temperature is too low, the error message will be displayed, and the user is advised to use the instrument at a higher temperature and to ensure the room temperature is between 54°F and 104°F . The user is advised to try again and to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite if the problem persists.
- **E-AB:** Temperature too high. If the temperature is too high, the error message will be displayed. The user is advised to ensure that the room temperature is between 54°F and 104°F and to make sure the instrument is not exposed to direct sunlight. The user is advised to try again and to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite if the problem persists.
- **G-AA:** Instrument error. If there is an error with the instrument, the error message will be displayed, and the user is advised to turn off and restart the instrument. The user is advised to try again and to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite if the problem persists.
- **G-AC:** Process error. The user is advised to repeat the test with a new test strip when the error message is displayed. The user is advised to try again and to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite if the problem persists.

- **G-AE:** Instrument error. When the error message is displayed, the user is advised to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite.
- **H-AC:** Low battery. If the battery is low, the error message will be displayed, and the user is advised to charge the instrument in the docking station.
- **H-AF:** Date/time lost. When the error message is displayed, the user is advised to enter the date and time before performing new tests.
- **H-AG:** Ejection error. The user is advised to eject the test strip using the eject button when the error message is displayed. The user is also advised to always use the eject button to remove the test strip to carefully remove the test strip manually if the test strip does not eject within 2 seconds.
- **S-AB:** Sample application error. If the sample is applied too early or after timing out, the error message will be displayed. The user is advised to repeat the test with a new test strip and to apply the sample when requested without moving the test strip.
- **S-AD:** Sample type error. If this error message is displayed, the user is advised to repeat the test with a new test strip and to ensure they are using one of the following sample types: arterial, venous, neonate arterial or neonate heel stick whole blood, or QC material for a QC test.
- **S-AF:** Sample error. The user is advised to repeat the test with a new test strip when the error message is displayed. The user is advised to try again and to contact their system administrator or they can contact Roche customer support if they do not have a system administrator onsite if the problem persists.
- **U-AE:** Invalid patient ID. If the patient ID is too long and/or contains invalid characters, the error message is displayed. The user is advised to re-enter the patient ID.
- **U-AG:** Unexpected bottle. When the error message is displayed, the user is advised to first Scan bottle: QC, Level 1 or Scan bottle: QC, Level 2 then scan the requested bottle again. The user is advised to contact their Roche representative if the problem persists.
- **'HI'**: is displayed when the glucose test result is greater than 600 mg/dL.
- **'LO'**: is displayed when the glucose test result is less than 10 mg/dL.

b. External control material:

i. The use of external quality control material is recommended to demonstrate that the cobas pulse system is working properly. The labeling states that the user should perform quality control testing only with the Roche QC (cobas® GLU QC kit) Solutions.

ii. The frequency of running quality controls is stated in the labeling. It is recommended to run both levels of quality controls at least once every 24 hours of patient testing and when one of the following occurs:

- the first time before using the instrument for patient testing,
- the first time the instrument is used by the operator,

- at shorter QC intervals if established by the workplace,
- when a new test strip container is opened,
- if there is a doubt about patient's glucose result,
- to test correct performance of the system,
- if the instrument was dropped,
- when other problems are suspected or identified (e.g., instrument outside of environmental conditions)

iii. A QC Lockout period ensures that QC is run frequently. By default, the QC lockout configuration is set to every 24 hours. The instrument cannot be used for patient testing while the device is in QC Lockout. QC tests must be completed successfully before the instrument can be used for glucose testing.

iv. Directions for use are clearly stated in the labeling (QRG, user guide and test strip insert).

v. Storage and stability are stated in the labeling. The user should follow the manufacturer's instructions for storage and stability. An error code (D-AE) is displayed if the QC material has expired.

vi. Two levels of ready-to-use liquid control solutions are available for use (Level 1, Level 2)

vii. Manufacturer: Roche

3. Flex Studies

The robustness of the cobas pulse glucose monitoring system was previously demonstrated in CW220002 where its operational limits were stressed due to potential operator errors, factors affecting specimen or test system integrity, or environmental factors. The only modification to the cobas pulse glucose monitoring system is the addition of the venous whole blood specimen type, therefore, no new flex studies were conducted. Please refer to FDA Decision Summary for CW220002 for more details.

L. Demonstrating "Insignificant Risk of an Erroneous Result" – Accuracy

The demonstration of an insignificant risk of erroneous results with the cobas pulse glucose monitoring system using arterial whole blood, neonatal arterial whole blood and neonatal heel stick whole blood was previously established in CW220002 which was also used to support FDA clearance under K220272.

To demonstrate that the cobas pulse glucose monitoring system poses an insignificant risk of erroneous results with venous whole blood in the hands of intended users and when performed in CLIA waived settings, the sponsor submitted a clinical study using venous whole blood which was also used to support FDA clearance under K252323.

1. Comparison Study

a. Study Design

i. Study Sites

The performance of the cobas pulse glucose monitoring system was assessed in professional healthcare settings at 7 clinical sites that included the general ward, operating rooms, medical intensive care units, surgical intensive care units, and pediatric intensive care units.

ii. Operators

Results from the cobas pulse glucose monitoring system were obtained during the clinical study by a total of 28 untrained operators who were untrained in the use of the cobas pulse glucose monitoring system.

iii. Instructions for Use

The operators were given the user guide, test strip insert, and the Quick Reference Guide. The operators received no other materials, instructions nor training in the use of the test.

iv. Subjects (Patients)

A total of 643 patients were enrolled and participated in the study. Venous samples from patients 1 year old to over 81 years of age were analyzed throughout the study. The glucose levels of the patient samples (according to the comparator) ranged from 26.1 to 482.6 mg/dL for all venous samples (156 samples <80 mg/dL and 14 samples >300 mg/dL). In addition to glucose levels, patient conditions, medication information, pO2, sodium, and hematocrit were collected during the study. This study included patients with 665 different patient conditions and diagnoses. Patients received a total of 616 different medications administered within 24 hours of blood draw. Please refer to the K252323 decision summary for a detailed list of patient medications and medical conditions.

v. Samples

Lithium heparin venous whole blood samples.

vi. Comparative Method (CM)

Roche Glucose HK Gen.3 assay (K191899) on the cobas 6000 system (K060373)

b. Results and Analysis

i. Data Analysis

1. The results of the cobas pulse glucose monitoring system were compared with those obtained on the comparator and are as follows:

Venous Whole Blood (combined)

Glucose concentrations < 75 mg/dL

Within ± 5 mg/dL	Within ± 10 mg/dL	Within ± 12 mg/dL	Within ± 15 mg/dL	Exceeds ± 15 mg/dL
93/110 (84.5%)	109/110 (99.1%)	110/110 (100.0%)	110/110 (100.0%)	0/110 (0.0%)

Glucose concentrations ≥ 75 mg/dL

Within ± 5 %	Within ± 10 %	Within ± 12 %	Within ± 15 %	Within ± 20 %	Exceeds ± 20 %
444/533 (83.3%)	524/533 (98.3%)	529/533 (99.2%)	533/533 (100.0%)	533/533 (100.0%)	0/533 (0.0%)

Capillary Fingerstick Whole Blood Limitations

The sponsor includes limitations against the use of the cobas pulse glucose monitoring system with capillary fingerstick whole blood. The labeling states the following limitations:

- This system is not intended for use with capillary finger stick whole blood, neonate cord blood specimens or neonate venous specimens.

- In comparing capillary whole blood glucose measurements using the cobas® pulse to venous plasma measurements using the comparator method, a large percentage of samples had significant bias to the comparator method.

These limitations were put in place due to risks posed by the performance of the cobas pulse glucose monitoring system with capillary fingerstick samples. The results of this device were compared with those obtained on the comparator method and are as follows:

For capillary fingerstick samples, 54.5% (12/22) of samples with glucose concentrations <75 mg/dL were within ±12 mg/dL and 45.5% (10/22) exceeded a difference of ±15 mg/dL relative to the comparator method result. Additionally, for capillary fingerstick samples with glucose concentrations ≥75 mg/dL, 82.2% (562/684) of the samples were within ±12 mg/dL and 7.0% (48/684) exceeded a difference of ±20% relative to the comparator method results.

ii. Allowable Total Error (ATE) and Limits for Erroneous Results (LER)

The study performed to support CLIA waiver for the cobas pulse glucose monitoring system was analyzed to evaluate whether the clinical data would meet clinically appropriate ATE and LER zones for the sponsor's intended use population. The analysis demonstrates that the percentage of results over the entire measurement range that falls within the ATE zone (within ±12 mg/dL for glucose concentrations < 75 mg/dL or within ±12% for glucose concentrations ≥75 mg/dL) is ≥95%. None of the results were in the LER zone.

1. Operator Questionnaire

Upon completion of the clinical studies, operators completed a questionnaire to evaluate the ease of understanding of the test procedure. The participants found the cobas pulse glucose monitoring system easy to use and the instructions in the user guide and QRG clear and easy to follow.

M. Labeling for Waived Devices

The labeling consists of:

1. Quick Reference Instructions
2. User Guide that contains information for the CLIA waived user
3. Test Strips Package Insert
4. Test strip box
5. Instrument box
6. User Assistance that contains information for the non-CLIA waived user
7. Addendum to the User Guide manual with clinical study information (medical conditions, medications etc.) for the non-CLIA waived user.

The following elements are appropriately present:

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

- The User Guide, Test Strip Package Insert and Quick Reference Guide for the CLIA waived user:
  - are written at no higher than a 7th grade reading level.
  - identify the test as CLIA waived.
  - contain a statement that a Certificate of Waiver is required to perform the test in a waived setting.

- contain a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test as required per 42 CFR 493.15(e)(1).
- provide instructions for conducting quality control procedures.

N. Conclusion:

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