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

A. 510(k) Number:

k133741

B. Purpose for Submission:

New device – Combining the previously cleared Inform II test strips (k121679; with a modified GDH-PQQ methodology) with the previously cleared Performa meter (k070585)

C. Measurand:

Venous and capillary whole blood glucose from the fingertip

D. Type of Test:

Quantitative amperometric assay, glucose dehydrogenase (mutant GDH-PQQ)

E. Applicant:

Roche Diagnostics Corporation

F. Proprietary and Established Names:

ACCU-CHEK Performa Blood Glucose Monitoring System

G. Regulatory Information:

1. Regulation section:
   21 CFR 862.1345, Glucose test system

2. Classification:
   Class II

3. Product code:
   NBW, System, Test, Blood Glucose, Over the Counter
   LFR, Glucose Dehydrogenase, Glucose

4. Panel:
   Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):
   See Indications for Use below.

2. Indications(s) for use:

   The ACCU-CHEK Performa Blood Glucose Monitoring System is intended to be used for the quantitative measurement of glucose (sugar) in venous whole blood or fresh capillary whole blood from the fingertips. The ACCU-CHEK Performa Blood Glucose Monitoring System is intended for testing outside the body (in vitro diagnostic use) and is intended for multiple-patient use in professional healthcare settings as an aid in monitoring the effectiveness of glucose control. This system should only be used with single-use, auto-disabling lancing devices.

   The ACCU-CHEK Performa Blood Glucose Monitoring System should not be used for the diagnosis of or screening for diabetes. This system is also not for neonatal use.

   The ACCU-CHEK Performa test strips are for use with the ACCU-CHEK Performa meter to quantitatively measure glucose (sugar) in venous whole blood or fresh capillary blood samples from the fingertips.

3. Special conditions for use statement(s):
   - For in vitro diagnostic use only
   - Not for use in diagnosis or screening of diabetes mellitus
   - Not for neonatal use
   - If peripheral circulation is impaired, collection of capillary blood from the approved sample sites is not advised as the results might not be a true reflection of the physiological blood glucose level. This may apply in the following circumstances: severe dehydration as a result of diabetic ketoacidosis or due to hyperglycemic hyperosmolar non-ketotic syndrome, hypotension, shock, decompensated heart failure NYHA Class IV, or peripheral arterial occlusive disease.
   - The performance of this meter has not been evaluated on critically ill patients.
   - For use with single-use, auto-disabling lancing devices

4. Special instrument requirements:

   ACCU-CHEK Performa Meter

I. Device Description:

The ACCU-CHEK Performa Blood Glucose Monitoring System consists of a the ACCU-CHEK Performa meter, ACCU-CHEK Performa test strips (sold separately; code key provided in test strip vials), ACCU-CHEK Inform II control solutions (Levels 1 and 2; sold

separately), ACCU-CHEK Inform II Linearity Test Kit (6 levels; sold separately), and Operator's Manual.

The enzyme on the test strip is a mutant variant of quinoprotein glucose dehydrogenase (Mut. Q-GDH), from Acinetobacter calcoaceticus, recombinant in E. coli. and uses Nitrosoaniline as a mediator.

Each box of ACCU-CHEK Inform II control solutions contains one vial (2.5 mL) of each of the 2 buffered aqueous solutions containing D-glucose: Level 1 and Level 2. These control solutions were previously cleared in k121679.
The ACCU-CHEK Inform II Linearity Test Kit contains 2.5 mL of each of the 6 buffered aqueous solutions containing D-glucose: (ACCU-CHEK Linearity 1-6, These linearity solutions were previously cleared in k121679.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ACCU-CHEK Inform II Blood Glucose Monitoring System

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

   k121679

3. Comparison with predicate:

Similarities		
Item	Predicate (k121679)	Candidate Device
Brand Name	**ACCU-CHECK Inform II**	**ACCU-CHEK Performa**
Indications for Use/Intended Use	To quantitatively measure glucose (sugar) in whole blood, as an aid in monitoring the effectiveness of glucose control.	Same
Enzyme	Glucose Dehydrogenase – PQQ modified by site-directed mutagenesis (Mutant Q-GDH)	Same
Test Principle	Amperometric detection	Same
Measuring time	5 sec	Same
Sample volume	0.6 μL	Same
Hematocrit range	10-65%	Same
Altitude claim	Up to 10,000 feet	Same
Coding	Lot-specific blood glucose measurement parameters are programmed into code key	Same

Differences		
Item	Predicate (k121679)	Candidate Device
Brand Name	**ACCU-CHECK Inform II**	**ACCU-CHEK Performa**
Measurement range	10-600 mg/dL	20-600 mg/dL
Sample Site	Venous, arterial, capillary fingerstick and neonate heelstick	Venous, and capillary fingerstick
Code Key Port	Code key inserts into code key reader which transfer data to meter via IR communication	Code key inserts directly into code key slot in meter
Battery	3.7 V rechargeable battery pack (lithium technology)	One 3-volt lithium type CR2032 coin cell
Bar Code Scanner	Yes	None
Transmission of Retrospective Data to External Devices	Wirelessly to WLAN through RF communication or to docking station base unit through IR data port	None
Meter Physical Appearance	7.60 in x 3.74 in x 1.73 in (LWH), 0.83 lbs	3.7 in x 2.1 in x 0.9 in (LWH), 0.14 lbs

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

- ISO 15197: In vitro diagnostic test systems - Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.
- CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline.
- CLSI EP7-A2, Interference Testing in Clinical Chemistry; Approved Guideline.

L. Test Principle:

The test is based on electrochemical biosensor technology and the principle of capillary action. The electrical current generated by the reaction of glucose with the reagent of the strip is measured by the meter and is displayed as the corresponding blood glucose level. The strength of the current produced by the reaction depends on the amount of glucose in the blood sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

Repeatability studies were performed with venous whole blood samples at five glucose concentration ranges using 3 test strip lots. Ten runs were performed on each sample with 5 replicates per run/strip lot resulting in a total of 100 replicates collected for each test strip lot and each glucose level tested. Results are summarized below:

Glucose Level	30-50 (mg/dL)			50-110 (mg/dL)			110-150 (mg/dL)		
Test Strip Lot	1	2	3	1	2	3	1	2	3
Mean (mg/dL)	36.7	36.6	37.1	79.1	78.9	81.1	132.5	131.6	134.6
SD	1.6	1.4	1.7	2.6	3.2	2.7	4.5	4.8	4.4
CV%	4.4	3.7	4.7	3.3	4.1	3.4	3.4	3.6	3.3
n	100	100	100	100	100	100	100	100	100

Glucose Level	150-250 (mg/dL)			250-400 (mg/dL)		
Test Strip Lot	1	2	3	1	2	3
Mean (mg/dL)	213.6	208.6	216.2	342.9	336.4	345.3
SD	7.6	7.8	7.9	11.9	11.8	10.2
CV%	3.6	3.7	3.6	3.5	3.5	3.1
n	100	100	100	100	100	100

Intermediate precision was evaluated using three glucose linearity solutions, Level 2, Level 3, and Level 4. Ten strip vials, from three test strip lots, were assigned to each of the three linearity levels. From each strip vial, a test was performed on each of the 3 linearity level solutions for 10 days. A total of 10 replicates were collected per vial, strip lot, and glucose level tested for a total of 300 measurements per glucose level. Results are summarized below:

Glucose Level	Level 2 (45 mg/dL)			Level 3 (118 mg/dL)			Level 4 (307 mg/dL)		
Test Strip Lot	1	2	3	1	2	3	1	2	3
Mean (mg/dL)	45.5	45.6	45.8	118.2	118.9	118.8	310.4	310.5	310.8
SD	1.1	1.2	1.5	2.5	2.9	2.7	5.6	6.7	6.6
CV%	2.3	2.7	3.2	2.1	2.4	2.3	1.8	2.1	2.1
n	100	100	100	100	100	100	100	100	100

b. Linearity/assay reportable range:

Linearity was evaluated using 3 test strip lots and 11 venous blood samples ranging in glucose concentrations from 1.7 to 583.2 mg/dL (1.7, 16.2, 38.3, 57.1, 85.2, 114.8,

144.4, 191.0, 293.2, 440.0, and 583.2 mg/dL). Three runs were performed on each sample, on each strip lot, with replicates of 8 for each run and test strip lot resulting in a total of 24 replicates for each test strip lot and glucose level tested. The values from the Performa meter were compared with those obtained from the reference method. The results from regression analysis are summarized below:

Lot #1: $y=1.038\ x+3.08$; $R^2 = 0.998$
Lot #2: $y=1.028\ x+2.14$; $R^2 = 0.998$
Lot #3: $y=1.003\ x+2.8614$; $R^2 = 0.998$

The results of the study support the sponsor's claimed glucose measurement range of 20 to 600 mg/dL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):
According to the sponsor, the ACCU-CHEK Performa system is traceable to the NIST SRM 917 glucose reference material. A method comparison was performed using the candidate device and a hexokinase method (Hitachi 917) as the reference method (see Section 2.a.)

Value Assignment for Control Solutions and Linearity Set: The previously cleared (k121679) ACCU-CHEK Inform II control solutions (Levels 1 and 2) and 6 levels of the ACCU-CHEK Inform II Linearity Test Kit (Levels 1 to 6) are available for use with the ACCU-CHEK Performa test system. The Linearity Solutions levels 2 and 4 are the same as the Control solution levels 1 and 2, respectively. Value assignment for the control solutions and linearity set is established for the ACCU-CHEK Performa test system and is based on the mean of repeated measurements compared to the established target values for each level. The target values for the linearity levels are provided in the linearity kit package insert and the control solution ranges are printed on the test strip vial label.

Control Solution and Linearity Set Stability: Protocols and acceptance criteria for open vial and closed vial (shelf-life) stability for the control solutions and linearity set solutions were previously reviewed and found to be acceptable under k121679. The labeling claims are 24 month shelf life stability and 3 month open-vial stability when stored at the recommended storage temperatures of 39°F to 86°F (4°C to 30°C). Labeling instructs the user not to freeze the solutions.

The protocols and acceptance criteria for the ACCU-CHEK Inform II test strips were previously reviewed and found to be acceptable under k121679. The sponsor claims closed-vial (shelf life) and open-vial stability of 18 months when stored at 39-86°F (4-30°C). The labeling instructs the users not to freeze the test strips.

c. Detection limit:
The reportable range for the ACCU-CHEK Performa Blood Glucose Monitoring System is 20 to 600 mg/dL. This range was verified by the linearity study (M.1.b).

d. Analytical specificity:

To assess potential interference the sponsor used venous whole blood samples adjusted to 2 different glucose levels of 55 and 350 mg/dL, split into a control sample and a test sample. Various endogenous and exogenous substances were then added to the test sample only. The % difference between the test and control sample was calculated and highest concentration tested at which no significant interference was observed is presented in the table below:

Potential Interfering Substance	**Concentration at which no significant interference is observed (mg/dL)**		**Potential Interfering Substance**	**Concentration at which no significant interference is observed (mg/dL)**
Amoxicillin	600		L-Cysteine	5
Ascorbic Acid	3		L-Glutathione, oxidized	183.9
Captopril	0.5			
Chlorpropamide	80		L-Glutathione, reduce	12.3
Cholesterol	500		Maltose	360
Cimetidine	10		L-dopa	2.0
Citric Acid	30		MethyldopaL-dopa	1.5
Conjugated Bilirubin	15		Naproxen	100
Diltiazem	20		Oxalic Acid	20
Dopamine	0.09		Potassium Chloride	50
Ethanol	350		Probenecid	60
Furosemide	6		Sodium Bicarbonate	336
Galactose	15		Tolazamide	200
Gamma Globulins	3000		Tolbutamide	100
Gentistic acid	50		Triglycerides	1800
Glucosamine	450		Xylose	100
Hemoglobin	500			

The sponsor has the following limitations in their labeling:

- Lipemic samples (triglycerides) in excess of 1800 mg/dL may produce elevated results.
- Intravenous administration of ascorbic acid which results in blood concentrations of ascorbic acid > 3 mg/dL will cause overestimation of glucose results.

- Blood concentrations of galactose >15 mg/dL will cause overestimation of blood glucose results.
- Maltose testing at 60 mg/dL of glucose has bias of 6.9 with 300 mg/dL maltose, bias of 7.6 with 360 mg/dL maltose and 10.5 with 500 mg/dL maltose

e. Assay cut-off:
Not Applicable.

2. Comparison studies:
   a. Method comparison with predicate device:

To assess system accuracy, results from the ACCU-CHEK Performa Blood Glucose Monitoring System were compared to a reference method, PCA-HK (Hitachi 917). Capillary samples from 105 participants with glucose with concentrations ranging from 34-582 mg/dL glucose obtained on the reference were measured on three test strip lots. Samples <50 mg/dL and > 463 mg/dL were altered by glycolysis or spiking. The results relative to reference are summarized in the tables below:

Performa Fingerstick vs. Reference
For glucose concentrations <75 mg/dL

lot	within ± 5 mg/dL	within ± 10 mg/dL	within ± 15 mg/dL
#1	17/19 (89.5%)	19/19 (100%)	19/19 (100%)
#2	15/19 (78.9%)	19/19 (100%)	19/19 (100%)
#3	17/19 (89.5%)	18/19 (94.7%)	19/19 (100%)

For glucose concentrations ≥ 75 mg/dL

lot	within ± 5 %	within ± 10 %	within ± 15 %	within ± 20 %
#1	56/86 (65.1%)	79/86 (91.9%)	84/86 (97.7%)	85/86 (98.8%)
#2	53/86 (61.6%)	78/86 (90.7%)	86/86 (100%)	86/86 (100%)
#3	50/86 (58.1%)	78/86 (90.7%)	84/86 (97.7%)	85/86 (98.8%)

Linear regression results Performa capillary vs. whole blood PCA-HK reference (N=105 of each of 3 test strip lots):
Lot #1 (34-582 mg/dL): y = 1.052x – 3.0; r =0.997
Lot #2 (34-582mg/dL): y = 1.034x + 0.1; r =0.997
Lot #3 (34-582 mg/dL): y = 1.049x – 2.0; r =0.996

Venous Study:
To assess the performance of the ACCU-CHEK Performa Blood Glucose Monitoring System using venous blood, 427 venous samples (lithium heparin) were used that contained glucose concentrations of 28 to 557 mg/dL (as measured by the reference method). The results obtained from the Performa system using 3 test strip lots were compared to results obtained using the reference method (PCA-HK) and are summarized below:

For glucose concentrations <75 mg/dL

lot	within ± 5 mg/dL	within ± 10 mg/dL	within ± 15 mg/dL
#1	26/29 (89.7%)	29/29 (100%)	29/29 (100%)
#2	26/29 (89.7%)	29/29 (100%)	29/29 (100%)
#3	24/29 (82.8%)	29/29 (100%)	29/29 (100%)

For glucose concentrations ≥ 75 mg/dL

lot	within ± 5 %	within ± 10 %	within ± 15 %	within ± 20 %
#1	286/398 (71.9%)	380/398 (95.5%)	394/398 (99.0%)	397/398 (99.7%)
#2	243/398 (61.1%)	372/398 (93.5%)	394/398 (99.0%)	398/398 (100%)
#3	251/398 (63.1%)	371/398 (93.2%)	396/398 (99.5%)	398/398 (100%)

Linear regression results Performa venous vs. whole blood PCA-HK reference (N=427 of each of 3 test strip lots):

Lot #1: $y = 1.041x – 3.3$; $r = 0.995$
Lot #2: $y = 1.064x – 4.1$; $r = 0.996$
Lot #3: $y = 1.051x – 3.1$; $r = 0.996$

b. Matrix comparison:

Anticoagulant study:
Venous blood was drawn from ten donors having glucose levels in 5 different glucose bins: <70, 71-110, 111-150, 151-250, >251 mg/dL. The donor blood was collected into each of 4 vacutainer tubes (lithium heparin, sodium heparin, EDTA, and sodium fluoride/potassium oxalate) and into vacutainer tubes containing no anticoagulant. Each anticoagulant was tested in replicates of sixteen. Results of the study demonstrate no significant bias when results from samples containing EDTA, lithium heparin, or sodium heparin were compared to results from samples containing no anticoagulant and support the use with the ACCU-CHEK Inform II system.

The sponsor includes the following limitation in the labeling: Iodoacetate or fluoride-containing anticoagulants are not recommended.

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):

User Performance Study:
To assess the performance of the ACCU-CHEK Performa Blood Glucose Monitoring System in the hands of lay users the sponsor performed a study with 192 lay user participants. Results were analyzed by comparing blood glucose results from the ACCU-CHEK Performa meter obtained by the lay user against the reference method value (PCA-HK). The samples ranged from 47 to 576 mg/dL as measured by the reference method. The results are summarized in the tables below:

Lay-user Performa vs. PCA-HK reference:

For glucose concentrations <75 mg/dL

within ± 5 mg/dL	within ± 10 mg/dL	within ± 15 mg/dL
23/31 (74.2%)	31/31 (100%)	31/31 (100%)

For glucose concentrations ≥ 75 mg/dL

within ± 5 %	within ± 10 %	within ± 15 %	within ± 20 %
74/161 (46%)	127/161 (78.9%)	157/161 (97.5%)	161/161 (100%)

Regression Analysis lay-user Performa vs. Ref: $y = 0.924x+4.0$; $r=0.992$

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:

Time of day	People without diabetes
Fasting and before meals	<100 mg/dL
2 hours after meals	<140 mg/dL

(1) American Diabetes Association: Standards of Medical Care in Diabetes-2013. Diabetes Care, 36, (Suppl. 1), S11-S66, 2013.

(2) *Tietz Fundamentals of Clinical Chemistry, 6th Edition*, Edited by Burtis CA and Ashwood ED, W. B. Saunders Co., Philadelphia, PA, 2008, p. 849.

N. Instrument Name:

ACCU-CHEK Performa Blood Glucose Meter

O. System Description:

1. Modes of Operation:

   Each test strip is single use and must be replaced with a new strip for additional readings.

   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 _____ or No __X__.

2. Software:

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

   Yes __X__ or No _____.

   The applicant has provided documentation that indicates the device was designed and developed under good software life-cycle processes.

3. Specimen Identification:

   Samples are applied directly to the test strip as they are collected. The ACCU-CHEK Performa meter memory stores up to 500 glucose test results with the time and date of the test and up to 20 control solutions results. Individual patient results cannot be identified. The labeling states that using memory data from meters used for multiple-patient testing is not recommended.

4. Specimen Sampling and Handling:

   This device is intended to be used with capillary whole blood from the fingertip and venous whole blood. There is not patient identification with this system.

5. Calibration:
   The system contains a code key included in each vial of test strips and is inserted into the meter. The code key contains the test strip code information specific to that test strip lot number.

6. Quality Control:
   The ACCU-CHEK Inform II Control Solutions are used as quality control checks to make sure that the ACCU-CHEK Performa system and ACCU-CHEK Performa test strips are working correctly. The labeling provides instructions on when quality control testing should be performed. Once the control solution result is displayed on the meter a control bottle symbol and a flashing L are displayed prompting the user to select the control solution level that was used.

   Control solution results are not included in the 14 and 30 day averages.

   The Warning box language in the Operator's Manual (page 29 and 41) states: "Individual patient results cannot be identified. Using memory data from meters used for multiple-patient testing is NOT recommended" and "Individual patient results cannot be identified. Transferring data from meters used for multiple-patient testing is NOT recommended", respectively.

   The ACCU-CHEK Inform II Linearity Test Kit

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

1) Hematocrit study:
   The effect of different hematocrit levels was evaluated using venous whole blood samples with hematocrit levels of 10 – 65% (10,15, 20, 25, 30, 43, 50, 55, 60, and 65%) spiked with glucose to achieve target concentrations of 25, 55, 120, 350, and 500 mg/dL. A total of 30 replicates were performed for each combination of strip lot, glucose concentration, and hematocrit level tested. The results demonstrated that the ACCU CHEK Performa Blood Glucose Monitoring System produces accurate results over the claimed hematocrit range of 10 – 65%.

2) Altitude study:
   To evaluate the effects of altitude on the Performa system results, venous blood samples from three donors were altered to 5 glucose concentrations (35, 60, 160, 350 and 500 mg/dL) and tested at 10,150 feet above sea level. The meter results were compared to those obtained with the reference method (PCA-HK; Hitachi 917). The results demonstrate acceptable bias to the reference to support the claims in the labeling that altitudes up to 10,000 feet have no significant effect on blood glucose measurements from the ACCU-CHEK Performa Blood Glucose Monitoring System.

3) Temperature and humidity studies:
The sponsor performed temperature and humidity studies using venous blood samples at target glucose concentrations of 70, 120, and 250 mg/dL to evaluate temperatures ranging from 61-95°F (16-35°C) and relative humidity from 10-80%. Combinations of the claimed temperature and humidity operating conditions were evaluated and meter results compared to a reference method. The results support the claimed range of operating conditions: 61-95°F and 10-80% relative humidity.

4) Sample volume study:
The sponsor performed a sample volume study to support the claimed minimum sample volume requirement for the ACCU-CHEK Performa system (0.6 µL) using blood samples at three glucose concentrations (45, 120, 450 mg/dL). The system displays an error code when insufficient sample is detected. Results support the claimed sample volume of 0.6 µL.

5) Infection Control Studies: The device is intended for multiple-patient use. Disinfection efficacy studies were performed on the materials comprising the meter by an outside commercial testing laboratory demonstrating complete inactivation of hepatitis B virus (HBV) with the chosen disinfectant, Super Sani-Cloth (EPA registration #9480-4). Robustness studies were also performed by the sponsor demonstrating that there was no change in performance or external materials of the meter after 10,950 cleaning and disinfection cycles (21,900 wipes). The robustness studies were designed to simulate 3 years of multiple-patient use. Labeling was reviewed for adequate instructions for the validated cleaning and disinfection procedures.

6) Electromagnetic Compatibility (EMC) testing was performed and found to be adequate for the Accu-Chek Performa system.

7) ACCU-CHEK Customer Care Service Center is available 24 hours a day, 365 day a year by calling 1-800-440-3638.

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.