DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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December 19, 2016

ROCHE DIAGNOSTICS OPERATIONS
DAVID TRIBBETT
REGULATORY PROGRAM MANAGER
9115 HAGUE ROAD
INDIANAPOLIS, IN 46250

Re: K160571
Trade/Device Name: cobas c 513 Analyzer,
cobas c 513 Tina-quant HbA1cDx Gen.3 Assay
Regulation Number: 21 CFR 862.1373
Regulation Name: Hemoglobin Alc test system
Regulatory Class: II
Product Code: PDJ, JJE
Dated: December 08, 2016
Received: December 09, 2016

Dear David Tribbett:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
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and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K160571

Device Name
cobas c 513 Analyzer
cobas c 513 Tina-quant HbA1cDx Gen.3 Assay

Indications for Use *(Describe)*

The cobas c 513 clinical chemistry analyzer is a fully automated, standalone clinical chemistry analyzer intended for the in-vitro quantitative determination of analytes in body fluids.

The Tina-quant Hemoglobin A1cDx Gen.3 assay is intended for use as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. It is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche/Hitachi cobas c 513 clinical chemistry analyzer. HbA1c determinations are useful for monitoring of long-term blood glucose control in individuals with diabetes mellitus.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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cobas c 513 Tina-quant Hemoglobin A1cDx Gen.3 assay
510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

Submitter Name	Roche Diagnostics Operations (RDO)
Address	9115 Hague Road Indianapolis, IN, 46250, USA
Contact	David Tribbett Phone: (317)-521-2964 FAX: (317)-521-2324 Email: david.tribbett@roche.com
Date Prepared	January 31, 2016
Proprietary Names	**cobas c** 513 clinical chemistry analyzer Tina-quant Hemoglobin A1cDx Gen.3
Common Names	Analyzer, Chemistry (Photometric, Discrete), for clinical use Glycosylated Hemoglobin Assay
Classification Name	Discrete photometric chemistry analyzer for clinical use Hemoglobin A1c test system
Product Codes	JJE, 21 CFR 862.2160 PDJ, 21 CFR 862.1373
Predicate Device	COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay, K121291
Establishment Registration	1823260, Roche Diagnostics Corporation

1. DEVICE DESCRIPTION

Roche Diagnostics plans to introduce the **cobas c** 513 clinical chemistry analyzer, a new member of the Roche / Hitachi family of analyzers. It has been developed jointly by Roche Diagnostics and Hitachi High Technologies (HHT). It is a standalone, high volume Roche/Hitachi **cobas c** analyzer, that is to be used with the Tina-quant HbA1cDx Gen.3 Assay which is intended for use with human whole blood and hemolysate samples for monitoring of long term blood glucose control in individuals with diabetes mellitus and as "an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes".

Analyzer

The **cobas c** 513 analyzer is a fully automated, software controlled analyzer system for in vitro quantitative determination of analytes in human body fluids. The **cobas c** 513 analyzer system includes a control unit and an analyzer with a closed tube sampling functionality.

The **cobas c** 513 control unit includes a computer (PC) located in the sampler unit, a touchscreen monitor, soft-keyboard, a mouse (optional use), and a printer. The control unit is used to perform tasks on the analyzer and the PC runs the software that controls the analyzer.

The software manages all instrument functions, all system functions, and all information related to orders and results. The software offers a graphical user interface (GUI) to control all functions by the operator. The control unit contains System Control software including interfaces to a Medical Device Data System (cobas Link) and to the customer Laboratory Information System (LIS).

The analyzer is composed of the sampler unit and the analytical unit. The sampler unit is composed of the rack loading/unloading areas, a barcode reader, a rack rotor, a STAT port, and conveyor lines. It is used to load and unload racks, power on the system, access the PC, and manage the conveyance of samples to the analytical unit.

The analytical unit is comprised of the reagent area, the sample area, and the reaction disk. Samples are conveyed to the analytical unit from the sample unit for photometric analysis before being returned to the sample unit.

Assay

Anticoagulated whole blood is hemolyzed either manually or automatically prior to determination of HbAlc by a turbidimetric inhibition immunoassay. Liberated hemoglobin (Hb) in the hemolyzed sample is converted to a derivative having a characteristic absorption spectrum and measured bichromatically. The instrument calculates the % HbAlc from the HbAlc/Hb ratio according to a user selected protocol, either IFCC or NGSP protocols.

The assay offers separate applications that are specific to the sample types whole blood and hemolysate. The Whole Blood Application differs from the Hemolysate Application in the hemolyzing step. For the Whole Blood Application, whole blood samples are placed on the analyzer. Hemolysis occurs onboard the analyzer. For the Hemolysate Application, hemolyzed samples are placed on the analyzer. Hemolysis occurs manually before placing the samples onboard the analyzer. The two applications yield the same results.

Test principle

This method uses tetradecyltrimethyl-ammonium bromide (TTAB) as the detergent in the hemolyzing reagent to eliminate interference from leukocytes (TTAB does not lyse leukocytes). Hemolyzing reagent is part of the test system and is either placed on board the analyzer for the whole blood application or used manually for the hemolysate application. Sample pretreatment to remove labile HbA1c is not necessary. All hemoglobin variants which are glycated at the β-chain N-terminus and which have antibody-recognizable regions identical to that of HbA1c are determined by this assay. Consequently, the metabolic state of patients having uremia or the most frequent hemoglobinopathies (HbAS, HbAC, HbAE, HbAD) can be determined using this assay.

Hemoglobin A1c

The HbA1c determination is based on the turbidimetric inhibition immunoassay (TINIA) for hemolyzed whole blood.

Sample and addition of R1 (buffer/antibody):

Glycohemoglobin (HbA1c) in the sample reacts with anti-HbA1c antibody to form soluble antigen-antibody complexes. Since the specific HbA1c antibody site is present only once on the HbA1c molecule, formation of insoluble complexes does not take place.

Addition of R2 (buffer/polyhapten) and start of reaction:

The polyhaptens react with excess anti-HbA1c antibodies to form an insoluble antibodypolyhapten complex which can be determined turbidimetrically.

Hemoglobin

Liberated hemoglobin in the hemolyzed sample is converted to a derivative having a characteristic absorption spectrum which is measured bichromatically during the preincubation phase (sample + R1) of the above immunological reaction. A separate Hb reagent is consequently not necessary.

The final result is expressed as mmol/mol HbA1c or % HbA1c and is calculated from the HbA1c/Hb ratio as follows:

Protocol 1 (mmol/mol HbA1c acc. to IFCC): HbA1c (mmol/mol) = (HbA1c/Hb) × 1000

Protocol 2 (% HbA1c acc. to DCCT/NGSP): HbA1c (%) = (HbA1c/Hb) × 91.5 + 2.15

Standardization

Traceability: This method has been standardized against the approved IFCC reference method for the measurement of HbA1c in human blood and can be transferred to results traceable to DCCT/NGSP by calculation.

2. INDICATIONS FOR USE

The **cobas c** 513 analyzer is a fully automated, standalone clinical chemistry analyzer intended for the in-vitro quantitative determination of analytes in body fluids.

The Tina-quant Hemoglobin A1cDx Gen.3 assay is intended for use as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. It is an

in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche/Hitachi **cobas c** 513 clinical chemistry analyzer. HbA1c determinations are useful for monitoring of long-term blood glucose control in individuals with diabetes mellitus.

3. TECHNOLOGICAL CHARACTERISTICS

As the **cobas c** 513 analyzer is a new member of the Roche/Hitachi clinical chemistry instruments family, a comparison to the **cobas c** 501 analyzer is shown in the table below to compare the analyzer to other members of the Roche/Hitachi Clinical Chemistry instrument family.

Substantial Equivalence – Analyzer Similarities

Topic	cobas c 501	cobas c 513
	Basic features	
Intended Use	Fully automated clinical chemistry analyzer intended for the in vitro quantitative / qualitative determination of analytes in body fluids	The **cobas c** 513 is a fully automated, discrete clinical chemistry analyzer intended for the in-vitro quantitative determination of analytes in body fluids.
Measurement principle	Absorbance Photometry (enzymes, substrates, proteins, DAT, TDM) ISE Potentiometric (electrolytes)	Absorbance Photometry (enzymes, substrates, proteins, DAT, TDM) N/A
Reaction modes	Endpoint, Kinetic, Potentiometric	Same N/A
Throughput Photometry	Max 600 tests per hour without ISE	400 tests per hour
Throughput ISE Potentiometry	Max 600 tests per hour	N/A
Analyzer	Standalone module or multiple modules linked	Standalone analyzer
	Sample Handling	
Typical sample volumes	1.0 – 35 µL	S1: 1.5-25 µl S2: 1.5-6 µl Dependent on sample type
Sample types	Serum, plasma, urine, CSF and other depending on the chemistry test	Hemolysate, whole blood, Serum/Plasma, Urine
Sample handling system	Input of samples via core input buffer using universal sample racks	Closed Tube Sampling (CTS) on specified 5 position Racks (CTS Rack) and universal sample racks
Sample capacity On board	150	Same
Sample identification	Barcode	Same

Topic	cobas c 501	cobas c 513
	Reagent Handling	
Reagent volume	5 – 180 µL	15-150 µl
Reagent container (electrolytes)	Plastic bottles open	N/A
Reagent container (non-electrolytes)	Plastic bottles closed via pierceable screwcaps	Plastic bottles closed via screwcaps. The cap of the reagent bottle is decapped (opened) by operator
Reagent access	Reagent cassette caps pierced onboard by the instrument	Cassette caps to be opened before placing on instrument
Onboard storage Temperature	Refrigerated 5 -12 °C	Refrigerated 5-15°C
Reagent bottle / Cassette identification	Barcode	RFID
On board reagent storage capacity	60 rotor channels on 1 rotor to run 60 reagent kits in parallel	Same
System cycle time	6 sec	7.2 sec
Reagent mixing	Ultrasonic	Same
Auto rerun	Available	Same
Application information transfer to instrument	Via remote transfer or CD	Via remote transfer
	Pipetting System	
Sample and reagent Syringes	XY robotic	Same
Reagent probes	2 polished steel probes	Same
Sample probes	1 polished steel probe	2 polished steel probes
Probe cleaning	Automatic for all probes	Same
Liquid level detection (LLD) sample	Electrostatic	Electrostatic for open tubes (S1), no LLD for CTS (S2)
Liquid level detection reagent	Initial Cassette Volume Check (ICVC)	Electrostatic (Capacitance)
Clot detection	Provided	Same
	Test Reaction Chamber	
Temperature control	Circulating water bath at 37°C	Same
Cuvettes	Multiple use	Same
	Detection Information	
Spectrophotometer	Gradient photometer with discrete photodiodes in fixed array	Same
Light source	Tungsten/halogen	Same
Light path	5.6 mm	5 mm
Measuring unit	1	same
Wavelengths	340,376,415,450,480,505,546, 570, 600, 660,700,800 nm	Same
	Calibration and Quality Control	
Calibrators	Multiple use	Same
Calibration modes	Linear, nonlinear	Same
Calibration Stability	Typically each lot or 12 weeks for same reagent on board	For HbA1c: 4 weeks during shelf live
Online QC	Yes	No automatic QC, but QC timeout function
Control storage on instrument	In remote buffer at ambient temperature	none
Calibrator/control value transfer	Via remote transfer or CD	Via remote transfer

Topic	cobas c 501	cobas c 513
Internal quality management system	Available to monitor and validate test results	Same
	Software and Interfaces	
Host Interface	RS232C bi-directional	LAN/Ethernet
Printer	Laser	Any printer supported by the OS
Display	Keyboard + touch-screen Optional use of mouse	Keyboard + touch-screen: soft-keyboard; Optional use of mouse
Software	cobas 6000 modular system software	c 513 instrument software
Configuration	One or several analytical units with one PC and one Core	One stand-alone analytical unit with one PC
Units controlled	cobas c501 and cobas e601	513 analytical unit, one unit
Functions performed	Data input, sample processing, result calculation, result reporting, quality control	Same
PC (Controller Unit) functions	Data input (keyboard, disc), Data output (screen, printer)	Data input (keyboard, disc) no input from USB,DVD-RAM Data output (screen, printer + USB, DVD-RAM)
Core Unit functions	Realtime database, data input and output (via HOST Communication) control of sample conveyer	Same
Analytical Unit(s) function	Control of analytic processes (pipetting, incubation, detection) Primary Signal processing	Same
Data storage	Real time database in Core unit (storage of System and Application parameters, Calibration Data ,QC Data, Sample results, Alarm history)	Same
Software-controlled test countdown	Available	Same
Result calculation	Automated measuring of signal for kinetic and endpoint methods according to cycle time and automated calculation of concentrations via calibration curve	Same
User management	Yes	Same
Flagging of errors	Available	Same

Substantial Equivalence – Assay Similarities

While the c 513 analyzer is a new member of the Roche /Hitachi family of analyzers, none of the analyzers in this family have received 510(k) clearance for an HbA1c “aid in diagnosis” assay for both human whole blood and hemolysate sample types. Sample type is a key element of the intended use, which necessitates the COBAS Integra 800 Tina-quant Hemoglobin A1cDx Gen.2 to be the predicate device since it has been cleared for aid in diagnosis for both of these sample types.

Feature	Predicate Device: COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay K121291	Candidate Device: cobas c 513 Tina-quant HbA1cDx Gen.3 assay
Intended Use	This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.	This test is intended for use as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. It is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche/Hitachi **cobas c** 513 clinical chemistry analyzer. HbA1c determinations are useful for monitoring of long-term blood glucose control in individuals with diabetes mellitus.
Sample Types	Anticoagulated venous or capillary blood Acceptable anticoagulants for both the hemolysate and whole blood applications include: Li-Heparin K2-EDTA K3-EDTA Na-Heparin NaF/K-Oxalate NaF/Na_2-EDTA	Anticoagulated venous blood Acceptable anticoagulants for both the hemolysate and whole blood applications include: Li-Heparin K2-EDTA K3-EDTA EDTA/Fluoride
Instrument Platform	COBAS Integra 800 • Absorbance Photometry	Cobas c 513 • Same
Calibrator	Cfas HbA1c	Same
Calibration Frequency	Each lot, every 29 days, and as required following quality control procedures	29 days
Calibration Mode	Logit/log 5	Hb: linear HbA1c : RCM4
Controls	PreciControl HbA1c norm and path	Same
Reagent Stability	Unopened: • 2-8ºC until expiration date On-bard in use: • 2-8ºC for 28 days	Same
Reporting Units	% HbA1c NGSP/DCCT and mmol/mol IFCC	Same
Antibody	Polyclonal anti-HbA1c from sheep blood	Same

Feature	Predicate Device: COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay K121291	Candidate Device: cobas c 513 Tina-quant HbA1cDx Gen.3 assay
Test Principle	The anticoagulated whole blood specimen is hemolyzed automatically on the COBAS INTEGRA 800 analyzers with COBAS INTEGRA Hemolyzing Reagent Gen.2. This method uses TTAB as the detergent in the hemolyzing reagent to eliminate interference from leukocytes (TTAB does not lyse leukocytes). Sample pretreatment to remove labile HbA1c is not necessary. All hemoglobin variants which are glycated at the β-chain N-terminus and which have antibody-recognizable regions identical to that of HbA1c are determined by this assay. Consequently, the metabolic state of diabetic patients having uremia or the most frequent hemoglobinopathies (HbAS, HbAC, HbAE, HbAD) can be determined by this assay.	This method uses tetradecyltrimethyl-ammonium bromide (TTAB) as the detergent in the hemolyzing reagent to eliminate interference from leukocytes (TTAB does not lyse leukocytes). Sample pretreatment to remove labile HbA1c is not necessary. All hemoglobin variants which are glycated at the β -chain N-terminus and which have antibody-recognizable regions identical to that of HbA1c are determined by this assay. Consequently, the metabolic state of patients having uremia or the most frequent hemoglobinopathies (HbAS, HbAC, HbAE, HbAD) can be determined using this assay.
Determination of HbA1c	Turbidimetric immunoinhibition (TINIA). Antigen-antibody complexes are formed and excess Ab aggregate with polyhapten to form insoluble complexes	HbA1c determination is based on the turbidimetric inhibition immunoassay (TINIA) for hemolyzed whole blood. Glycohemoglobin in the sample reacts with anti-HbA1c to form soluble antigen-antibody complexes. Polyhaptens react with excess anti-HbA1c to form an insoluble antibody-polyhapten complex which can be measured turbidimetrically.
Determination of Hb	Bichromatic photometric determination after conversion to a colored derivate	Liberated hemoglobin in the hemolyzed sample is converted to a derivative having a characteristic absorption spectrum which is measured bichromatically.
Determination of % HbA1c	The final result is expressed as % HbA1c and is calculated from the HbA1c/Hb ratio per DCCT/NGSP as follows: HbA1c (%) = (HbA1c/Hb) × 91.5 + 2.15	Same
Claimed Measuring Range	Hemoglobin: • 4‑35 g/dL (2.48 – 21.7 mmol/L) HbA1c: • 0.3‑3.4 g/dL (0.186 – 2.11 mmol/L)	Hemoglobin: • 4-40 g/dL (2.48-24.8 mmol/L) HbA1c: • 0.3-1.93 g/dL (0.186-1.2 mmol/L)
Traceability	The assigned HbA1c and total hemoglobin values of the cobas c Tina-quant Hemoglobin A1c Gen.3 assay is certified with the National Glycohemoglobin Standardization Program (NGSP). The NGSP certification expires in one year.	Same

Feature	Predicate Device: COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay K121291	Candidate Device: cobas c 513 Tina-quant HbA1cDx Gen.3 assay
Reagent Composition	R1 Antibody Reagent: • MES(2-morpholinoethane sulfonic acid) buffer: 0.025 mol/L • TRIS (Tris(hydroxymethyl) aminomethane) buffer: 0.015 mol/L, pH 6.2 • HbA1c antibody (ovine serum): ≥ 0.5 mg/ml • detergents; stabilizers; preservatives SR Polyhapten Reagent: • MES buffer: 0.025 mol/L • TRIS buffer: 0.015 mol/L, pH 6.2 • HbA1c polyhapten: > 8µg/mL • stabilizers; preservatives A1CD (Hemolyzing Reagent): • Aqueous buffered matrix, pH 7.25 • Tetradecyltrimethylammonium bromide: 36 g/L • sodium dihydrogenphosphate monohydrate: 16 mmol/L • sodium monohydrogenphosphate dihydrate: 64 mmol/L stabilizers; preservatives	R1 Antibody Reagent: • MES(2-morpholinoethane sulfonic acid) buffer: 0.025 mol/L • TRIS (Tris(hydroxymethyl) aminomethane) buffer: 0.015 mol/L, pH 6.2 • HbA1c antibody (ovine serum): ≥ 0.5 mg/ml • detergents; stabilizers; preservatives R3 Polyhapten Reagent: • MES buffer: 0.025 mol/L • TRIS buffer: 0.015 mol/L, pH 6.2 • HbA1c polyhapten: > 8µg/mL • stabilizers; preservatives A1CD (Hemolyzing Reagent): • Aqueous buffered matrix, pH 7.25 • Tetradecyltrimethylammonium bromide: 36 g/L • sodium dihydrogenphosphate monohydrate: 16 mmol/L • sodium monohydrogenphosphate dihydrate: 64 mmol/L • stabilizers; preservatives

4. NON-CLINICAL PERFORMANCE EVALUATION

Performance characteristics were evaluated with the Tina-quant HbA1c Gen.3 reagent on the **cobas c** 513 analyzer.

This assay offers two sample type-specific applications, one for manually hemolysed samples and one for whole blood samples; thus they are named the Hemolysate and Whole Blood Applications.

The Tina-quant HbA1c Gen.3 assay first measures total hemoglobin (Hb) and glycated hemoglobin (HbA1c) in terms of mmol/L. Then the analyzer calculates the HbA1c/Hb ratio according to the corresponding protocol, either IFCC or DCCT/NGSP. IFCC protocol reports the ratio in terms of mmol/mol HbA1c while the DCCT/NGSP protocol reports the ratio in terms of % HbA1c. Performance characteristics that support the measuring ranges claimed for Hb and HbA1c include limit of detection and linearity. They report results in terms of Hb and HbA1c individually. A patient sample value is reported in terms of the ratio of glycated to total hemoglobin. Method comparison, control recovery, and precision are evaluated in terms of the ratio. The protocol according to DCCT/NGSP was chosen for these studies.

The following performance data were provided in support of the substantial equivalence determination:

4.1. Limit of Blank and Limit of Detection (LoB and LoD)

4.1.1. Limit of Blank

For determination of LoB one analyte free sample will be measured with three lots in 10-fold determination. Six runs distributed over ≥ 3 days using one c 513 analyzer will be performed. In total, 60 measurements will be obtained per lot. Data analysis will be based on determination of the 95th percentile of the 60 measured values. In our design (n=60) the 95th percentile is the average of the 57th and 58th value (see also EP17-A2).

4.1.2. Limit of Detection

For determination of LoD, five samples with low-analyte concentration will be measured with three lots in two-fold determination. Six runs distributed over ≥ three days on one c 513 analyzer will be performed. In total, 60 measurements will be obtained per lot.

LoD is defined as the concentration, at which there is a 95% probability that a sample contains analyte.

LoB and LoD Results

		Result (g/dL)	Result (mmol/L)
Limit of Blank	Hb	0.50	0.31
	HbA1c	0.19	0.12
Limit of Detection	Hb	1.00	0.62
	HbA1c	0.29	0.18

4.2. Precision

Precision experiments were performed in Accordance with CLSI Guideline EP5-A2 to evaluate repeatability (within-run precision) and intermediate precision of within-laboratory precision (total precision).

Two aliquots per sample were measured once each in two runs per day for 21 days on three **cobas c** 513 analyzers using 3 reagent lots per system. Eight total samples were evaluated in each run: two controls, PreciControl HbA1c norm and path, and 7 human samples with HbAc concentrations near 5%, 6.5%, 7.0%, 8.0%, 10.5%, 12%, and 14%.

The samples were randomized in each run separately. The data set was completed for the 21 days. For each sample, the following was calculated: mean, repeatability and intermediate precision as CV and SD values, and the upper 95% confidence interval for SD and CV values.

c513 (Hemolysate) - instrument 1										
Mean %HbA1c	**Repeatability**		**Between-run**		**Between-day**		**Between-lot**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.59%	0.02	0.5	0.02	0.4	0.02	0.4	0.02	0.3	0.04	0.8
Human2, 6.18%	0.03	0.4	0.00	0.0	0.02	0.4	0.02	0.4	0.04	0.7
Human3, 6.97%	0.03	0.4	0.01	0.1	0.02	0.4	0.03	0.5	0.05	0.7
Human4, 8.05%	0.03	0.3	0.02	0.2	0.03	0.3	0.06	0.7	0.07	0.9
Human5, 10.3%	0.04	0.4	0.01	0.1	0.03	0.3	0.05	0.5	0.08	0.7
Human6, 11.8%	0.05	0.5	0.05	0.4	0.05	0.4	0.07	0.6	0.11	0.9
Human7, 13.9%	0.06	0.5	0.03	0.2	0.06	0.4	0.00	0.0	0.09	0.7
Preci Norm, 5.40%	0.02	0.4	0.01	0.1	0.02	0.4	0.01	0.2	0.03	0.6
Preci Path, 10.4%	0.04	0.4	0.00	0.0	0.04	0.4	0.06	0.6	0.08	0.8

c513 (Hemolysate) - instrument 2										
Mean %HbA1c	**Repeatability**		**Between-run**		**Between-day**		**Between-lot**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.64%	0.02	0.5	0.02	0.5	0.02	0.4	0.01	0.3	0.04	0.02
Human2, 6.25%	0.03	0.4	0.01	0.1	0.03	0.4	0.02	0.4	0.05	0.03
Human3, 7.06%	0.03	0.4	0.00	0.0	0.03	0.4	0.03	0.4	0.05	0.03
Human4, 8.14%	0.03	0.4	0.00	0.0	0.03	0.4	0.04	0.4	0.06	0.03
Human5, 10.4%	0.04	0.4	0.01	0.1	0.04	0.4	0.05	0.5	0.08	0.04
Human6, 12.0%	0.08	0.6	0.04	0.3	0.06	0.5	0.11	0.9	0.15	1.3
Human7, 13.8%	0.05	0.4	0.04	0.3	0.04	0.3	0.07	0.5	0.10	0.05
Preci Norm, 5.46%	0.03	0.5	0.01	0.2	0.02	0.4	0.02	0.4	0.04	0.03
Preci Path, 10.5%	0.04	0.4	0.02	0.2	0.04	0.4	0.05	0.5	0.08	0.04

c513 (Hemolysate) - instrument 3										
Mean %HbA1c	**Repeatability**		**Between-run**		**Between-day**		**Between-lot**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.67%	0.02	0.5	0.03	0.7	0.01	0.3	0.03	0.6	0.05	1.1
Human2, 6.26%	0.03	0.4	0.02	0.3	0.02	0.3	0.03	0.5	0.05	0.8
Human3, 7.06%	0.03	0.4	0.03	0.4	0.02	0.2	0.04	0.6	0.06	0.9
Human4, 8.14%	0.03	0.4	0.02	0.2	0.03	0.4	0.07	0.8	0.08	1.0
Human5, 10.4%	0.04	0.4	0.02	0.2	0.03	0.3	0.09	0.9	0.11	1.1
Human6, 11.8%	0.06	0.5	0.03	0.2	0.04	0.4	0.09	0.7	0.12	1.0
Human7, 13.8%	0.06	0.4	0.05	0.3	0.04	0.3	0.09	0.7	0.13	0.9
Preci Norm, 5.49%	0.02	0.4	0.02	0.4	0.02	0.3	0.03	0.5	0.04	0.8
Preci Path, 10.5%	0.04	0.4	0.03	0.2	0.03	0.3	0.09	0.9	0.11	1.1

c513 Hemolysate - all 3 instruments												
Mean %HbA1c	**Repeatability**		**Between Run**		**Between Day**		**Between Lot**		**Between Instrument**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.63%	0.02	0.5	0.03	0.6	0.02	0.4	0.02	0.4	0.04	0.9	0.06	1.3
Human2, 6.23%	0.03	0.4	0.01	0.2	0.02	0.4	0.03	0.4	0.04	0.7	0.06	1.0
Human3, 7.03%	0.03	0.4	0.02	0.2	0.02	0.3	0.04	0.5	0.05	0.7	0.07	1.0
Human4, 8.11%	0.03	0.4	0.01	0.2	0.03	0.4	0.06	0.7	0.04	0.5	0.08	1.0
Human5, 10.4%	0.04	0.4	0.02	0.2	0.04	0.3	0.07	0.7	0.03	0.3	0.10	0.9
Human6, 11.9%	0.06	0.5	0.04	0.3	0.05	0.5	0.09	0.7	0.09	0.7	0.15	1.3
Human7, 13.8%	0.06	0.4	0.04	0.3	0.05	0.4	0.07	0.5	0.02	0.1	0.11	0.8
Preci Norm 5.45%	0.02	0.4	0.01	0.3	0.02	0.4	0.02	0.4	0.04	0.8	0.06	1.1
Preci Path, 10.4%	0.04	0.4	0.01	0.1	0.04	0.4	0.07	0.7	0.03	0.3	0.10	0.9

c513 (Whole Blood) - instrument 1										
Mean %HbA1c	**Repeatability**		**Between-run**		**Between-day**		**Between-lot**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.54%	0.03	0.6	0.02	0.5	0.01	0.3	0.07	1.5	0.08	1.7
Human2, 6.21%	0.02	0.4	0.01	0.1	0.02	0.3	0.01	0.2	0.03	0.6
Human3, 6.97%	0.03	0.4	0.01	0.2	0.02	0.3	0.01	0.2	0.04	0.6
Human4, 8.10%	0.04	0.5	0.01	0.1	0.03	0.4	0.04	0.5	0.06	0.8
Human5, 10.5%	0.04	0.4	0.04	0.4	0.01	0.1	0.09	0.8	0.10	1.0
Human6, 11.8%	0.05	0.4	0.04	0.4	0.08	0.6	0.10	0.8	0.14	1.2
Human7, 13.9%	0.06	0.5	0.06	0.4	0.05	0.4	0.06	0.4	0.12	0.8
Preci Norm, 5.42%	0.03	0.5	0.01	0.2	0.02	0.4	0.03	0.5	0.05	0.8
Preci Path, 10.6%	0.04	0.4	0.04	0.4	0.03	0.3	0.08	0.8	0.10	1.0

c513 (Whole Blood) - instrument 2										
Mean %HbA1c	**Repeatability**		**Between-run**		**Between-day**		**Between-lot**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.64%	0.03	0.6	0.03	0.7	0.01	0.2	0.02	0.4	0.05	1.0
Human2, 6.29%	0.03	0.4	0.01	0.2	0.02	0.3	0.02	0.3	0.04	0.6
Human3, 7.05%	0.03	0.5	0.03	0.5	0.01	0.1	0.02	0.2	0.05	0.7
Human4, 8.17%	0.04	0.5	0.03	0.4	0.02	0.3	0.05	0.6	0.07	0.9
Human5, 10.5%	0.05	0.5	0.03	0.3	0.02	0.2	0.07	0.6	0.09	0.8
Human6, 12.1%	0.07	0.6	0.04	0.3	0.07	0.6	0.15	1.3	0.19	1.5
Human7, 13.9%	0.06	0.4	0.05	0.3	0.08	0.6	0.13	0.9	0.17	1.2
Preci Norm, 5.51%	0.03	0.5	0.02	0.4	0.01	0.2	0.01	0.2	0.04	0.7
Preci Path, 10.6%	0.05	0.5	0.04	0.4	0.01	0.1	0.07	0.6	0.09	0.9

c513 (Whole Blood) - instrument3										
Mean %HbA1c	**Repeatability**		**Between-run**		**Between-day**		**Between-lot**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.61%	0.03	0.7	0.02	0.4	0.02	0.3	0.01	0.2	0.04	0.9
Human2, 6.27%	0.03	0.4	0.02	0.3	0.01	0.2	0.04	0.6	0.05	0.8
Human3, 7.04%	0.04	0.5	0.02	0.3	0.01	0.2	0.04	0.6	0.06	0.9
Human4, 8.21%	0.04	0.5	0.04	0.4	0.01	0.1	0.09	1.1	0.10	1.2
Human5, 10.6%	0.04	0.4	0.04	0.4	0.00	0.0	0.13	1.2	0.14	1.3
Human6, 12.0%	0.06	0.5	0.05	0.4	0.05	0.4	0.07	0.6	0.11	0.9
Human7, 13.8%	0.07	0.5	0.03	0.2	0.04	0.3	0.27	2.0	0.28	2.1
Preci Norm, 5.48%	0.03	0.5	0.01	0.2	0.01	0.3	0.01	0.3	0.04	0.7
Preci Path, 10.7%	0.05	0.5	0.06	0.6	0.00	0.0	0.13	1.2	0.15	1.4

c513 - whole blood - all 3 instruments												
Mean %HbA1c	**Repeatability**		**Between Run**		**Between Day**		**Between Lot**		**Between Instrument**		**Total**	
	SD	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**	**SD**	**%CV**
Human1, 4.60%	0.03	0.6	0.02	0.5	0.01	0.3	0.04	0.9	0.04	1.0	0.07	1.6
Human2, 6.26%	0.03	0.4	0.01	0.2	0.02	0.3	0.02	0.4	0.04	0.6	0.06	0.9
Human3, 7.02%	0.03	0.5	0.02	0.4	0.02	0.2	0.03	0.4	0.04	0.5	0.06	0.9
Human4, 8.16%	0.04	0.5	0.03	0.3	0.02	0.3	0.06	0.8	0.04	0.5	0.09	1.1
Human5, 10.5%	0.04	0.4	0.04	0.4	0.01	0.1	0.10	0.9	0.00	0.0	0.11	1.1
Human6, 12.0%	0.06	0.5	0.04	0.3	0.07	0.6	0.11	0.9	0.11	0.9	0.19	1.5
Human7, 13.9%	0.06	0.5	0.05	0.3	0.06	0.4	0.18	1.3	0.00	0.0	0.20	1.5
PreciNorm 5.47%	0.03	0.5	0.01	0.3	0.02	0.3	0.02	0.3	0.04	0.8	0.06	1.1
PreciPath, 10.6%	0.05	0.5	0.05	0.5	0.01	0.1	0.09	0.9	0.00	0.0	0.12	1.1

4.3. Method Comparison

A method comparison study was performed to compare the sample results from the candidate method, Tina-quant HbA1c Gen.3 on the **cobas c** 513, to results from the TOSOH 8 HPLC. This study will be conducted with both the Tina-quant HbA1c Gen.3 Whole Blood Application and Hemolysate Application.

One hundred and fifty-five (155) samples from the secondary NGSP reference laboratory were used in the evaluation. These samples were measured by the secondary NGSP reference laboratory using a Tosoh HPLC system (X axis) and by the Roche Tina-quant HbA1c Gen.3 test system (Y axis). Samples were tested over a 3 day period with one lot of reagent on one **cobas c** 513 analyzer.

All acceptance criteria for method comparison were met. The difference plots show there is good agreement between the Roche method and the NGSP TOSOH HPLC reference method. The table below summarizes the bias between the Tina-quant HbA1c Gen.3 (Whole Blood and Hemolysate applications) and the NGSP's TOSOH HPLC reference method.

Difference Plot Analysis Data Summary

	Tina-quant HbA1c Gen.3 Whole Blood Application	Tina-quant HbA1c Gen.3 Hemolysate Application
Mean bias vs. NGSP TOSOH	-0.016	-0.138
Mean bias at lower 95% CI	-0.260	-0.429
Mean bias at upper 95% CI	0.227	0.153

The table below summarizes the percent relative bias at various points in the measuring range for both applications.

Bias at Concentration Data Summary

%HbA1c	Bias limit	% Relative Bias Whole Blood Application	% Relative Bias Hemolysate Application
>5%	≤ 5.0%	0.1%	-0.8%
6.0%	≤ 3.5%	-0.2%	-1.4%
6.5%	≤ 3.5%	-0.3%	-1.6%
7.0%	≤ 3.5%	-0.4%	-1.8%
>12.0%	≤ 10%	-0.8%	-2.8%

Method Comparison Sample Distribution

Hemolysate		
% HbA1c	Samples Tested	% of Total
≤ 5%	6	3.9%
5 – 6%	25	16.1%
6 – 6.5%	30	19.4%
6.5 – 7%	36	23.2%
7– 8%	25	16.1%
8– 9 %	14	9.0%
> 9%	19	12.3%
Total	155	100.0%

Whole blood		
% HbA1c	Samples Tested	% of Total
≤ 5%	6	3.9%
5 – 6%	26	16.9%
6 – 6.5%	30	19.5%
6.5 – 7%	36	23.4%
7– 8%	25	16.2%
8– 9 %	14	9.1%
> 9%	17	11.0%
Total	154	100.0%

4.4. Total Error Near the Cut-off

Using the results of bias estimation (%Bias) in the method comparison study and precision estimates in the precision study, the Total Error (TE) at the following concentrations (5%, 6.5%, 8% and 12%) was calculated as follows: %TE =|%Bias| + 1.96 * %CV * (1+%Bias). The results are presented in the tables below.

Total Error - Whole Blood Application

% HbA1c	%BIAS	%CV	Total Error (%)
5.0% HbA1c	0.7	1.6	3.9
6.5% HbA1c	0.3	0.9	2.1
8.0% HbA1c	0.1	1.1	2.3
12.0% HbA1c	0.2	1.5	3.1

Total Error – Hemolysate Application

% HbA1c	%BIAS	%CV	Total Error (%)
5.0% HbA1c	1.1	1.3	3.7
6.5% HbA1c	1.7	1.0	3.7
8.0% HbA1c	2.0	1.0	4.0
12.0% HbA1c	2.6	1.3	5.2

4.5. Linearity

Two separate dilution series consisting of at least 11 levels were prepared using the human hemolysate sample pools with either HbA1c or Hb with concentrations above the upper end of the corresponding measuring range. Hemolyzing reagent was used for the diluent. Samples were measured in triplicate and data analysis was done separately for each sample. Linear regression analysis was done according to EP6-A. Additionally, first order regression statistics using theoretical values determined from sample pools with known concentrations is provided in the table below.

Empirical First Order Linear Regression Results

Application	Analyte	Low End of Linear Range		High End of Linear Range		Slope	Intercept	Pearson's r
		g/dL	mmol/L	g/dL	mmol/L			
Hemolysate	Hb	3.4	2.09	40.3	25.0	0.983	0.051	0.9999
	HbA1c	0.28	0.177	2.85	1.77	0.972	0.002	0.9990

Claimed Ranges:

Hemoglobin: 4.0 - 40 g/dL (2.48‑24.8 mmol/L)

HbA1c: 0.3 - 1.93 g/dL (0.186‑1.20 mmol/L)

This corresponds to a measuring range of 23‑146 mmol/mol HbA1c (IFCC) and 4.2‑15.5 % HbA1c (DCCT/NGSP) at a typical hemoglobin concentration of 8.2 mmol/L.

4.6. Matrix Comparison

A matrix comparison study was performed to evaluate different anticoagulants on analyte recovery. At least 40 samples of each sample type and at least 40 half-filled tubes of each sample type were evaluated. The half-filled (double concentrated) and filled sample tubes were from one donor. Only samples within the limit of icteric, lipemic and hemolytic interference

were used. Samples covered the measuring range. The Hemolysate application was used for these measurements. All acceptance criteria for matrix comparison were met.

Matrix Comparison Results

Sample Type	Anticoagulant	Tube Fill	Mean Difference	Upper 95%	Lower 95%
Hemolysate	K_2-EDTA	½ full	-0.0559	0.319	-0.431
	K_3-EDTA	Full	0.000732	00418	-0.417
		½ full	-0.0351	0.506	-0.576
	Li Heparin	Full	0.0156	0.501	-0.470
		½ full	-0.0285	0.504	-0.561
	NaF/Potox	Full	-0.00732	0.459	-0.473
		½ full	0.0393	0.483	-0.404

4.7. Endogenous Interference

A study evaluated several endogenous substances for potential interference with the measure of % HbA1c. The following six endogenous substances were evaluated:

- Lipemia
- Bilirubin
- Ditaurobilirubin
- Glucose
- Rheumatoid Factor
- Total Protein

Pooled whole blood samples with two A1c levels, one near the medical decision level and one above it, were spiked with the maximum level of the above six interferents in separate preparations resulting in 12 spiked samples. These samples were then hemolyzed with Tina-quant HbA1c Hemolyzing Reagent. Another pool, without interferent, was equally hemolyzed. A minimum of a 10-level dilution series was then created for each of the 12 spiked samples by using the interferent free pool as the diluting reagent.

The experiment was performed with one reagent lot, one c 513 analyzer, and in a single run from the same calibration. PreciControl HbA1c norm and path will be the controls. The twelve dilution series were tested ten-fold for % HbA1c using the Hemolysate Application only. Interference is a matter of specificity of the assay which is independent of the application; therefore, interference data on the Hemolysate application will be representative of data on both the Hemolysate and Whole Blood Applications.

The mean of the ten replicates was determined and compared to the result from the reference sample (aliquot with no interfering substance). The comparison was evaluated as a percent deviation. An interferent will be significant if it causes >7% deviation of a measurement in terms of % HbA1c.

Endogenous Interference

Interferent	Maximum Concentration without interference Claimed
Lipemia	600 mg/dL
Bilirubin	60 mg/dL
Ditaurobilirubin	60 mg/dL
Glucose	1000 mg/dL
Rheumatoid Factor	750 IU/mL

4.8. Drug Interferences

A study evaluated several drugs for potential interference with the measurement of %HbA1c using the hemolysate application. The following drugs were studied:

- N- Acetylcysteine
- Ampicillin-Na
- Ascorbic acid
- Cefoxitin
- Heparin
- Levodopa
- Methyldopa

- Metronidazole
- Doxycyclin
- Acetylsalicylic acid
- Rifampicin
- Cyclosporine
- Phenylbutazone
- Acetaminophen
- Ibuprofen
- Theophylline

The 16 commonly used drugs listed above were added to native patient samples and examined for potential effect on % HbA1c determination with the Hemolysate Application. Drug interference testing was performed with hemolysate samples at 2 different HbA1c levels. The two different HbA1c concentrations will be approximately 6% and 8% HbA1c. Each drug was added in two defined concentrations with concentration 1 being several times (typically 5 times) the maximum daily dosage and concentration 2 being the maximum daily dosage level. Concentration 1 was performed for screening purposes only and concentration 2 is the relevant drug concentration for determining interferences with the assay. Samples were measured in tenfold using the **cobas c** 513 system. The median value was compared to the reference value (HbA1c sample with no drug added) and the deviation from the reference was calculated.

The data was collected using the Hemolysate Application which is acceptable since the assay interference is a matter of specificity of the antibody.

Significant interference is defined as > ±7% deviation from the reference value observed. All acceptance criteria for drug interferences were met.

4.9. Cross reactivity

Studies were performed to determine if the Tina-quant Hemoglobin A1cDx Gen.3 assay demonstrates cross-reactivity with any of the following hemoglobin fractions and glycated albumin.

- HbA0
- HbA1a+b
- Acetylated Hb
- Carbamylated Hb
- Glycated Albumin
- Labile HbA1c

A series experiments were performed with one reagent lot, one c 513 analyzer, and in a single run from the same calibration. PreciControl HbA1c norm and path function as the controls. Ten replicates of each sample were analyzed. The % recovery of the median for each dilution step related to the median obtained for Pool 1 will be plotted against the dilution step and/or the concentration of the potential cross-reactant.

As with the interference studies, the data was collected using the Hemolysate Application only. This is acceptable because cross-reactivity is a matter of specificity of the assay which is independent of the application. Therefore, cross-reactivity data on the Hemolysate Application are representative of data on both the Hemolysate and Whole Blood Application.

Cross-Reactivity

Cross-Reactant		Max Concentration Measured	Max Concentration with no interference
HbA0	Level 1	120 g/dL	120 g/dL
	Level 2	120 g/dL	120 g/dL
HbA1a+b	Level 1	1.60 g/dL	0.96 g/dL
	Level 2	1.60 g/dL	1.60 g/dL
Acetylated Hb	Level 1	2.00 g/dL	2.00 g/dL
	Level 2	2.00 g/dL	2.00 g/dL
Carbamylated Hb	Level 1	2.0 g/dL	2.0 g/dL
	Level 2	2.0 g/dL	2.0 g/dL
Glycated albumin	Level 1	10.0 g/dL	10.0 g/dL
	Level 2	10.0 g/dL	10.0 g/dL
Labile HbA1c	Level 1	1500 mg/dL	1500 mg/dL
	Level 2	1500 mg/dL	1500 mg/dL

4.10. Hemoglobin Variants

Hemoglobin variant testing was conducted to determine if there was any significant interference with any of the major hemoglobin variants and the Tina-quant Hemoglobin A1cDx Gen.3 assay. Hemoglobin variants are structurally altered hemoglobin molecules with at least one amino acid exchange compared to the normal beta chain of hemoglobin. These changes are caused by mutations in the coding region of the globin genes which encode the protein part of hemoglobin. The most common hemoglobin variants are HbS, HbC, HbD and HbE. Moreover, in some conditions, the fetal hemoglobin HbF is elevated. Also, the erythrocytes of some patients (e.g. beta thalassemia minor) contain elevated levels of HbA2. Therefore, it is crucial to ensure accurate HbA1c results from patients who are carriers of these variants.

Hemoglobin Variant Samples

Variant Type	Number of Samples	% Variant	HbA1c %
HbS	20	31 – 42% S	5.0-14.4
HbC	20	33 – 44% C	4.7-13.0
HbE	20	27 – 33% E	5.0-9.7
HbD	20	34 – 42% D	5.0-10.9
Elevated F	20	2 – 28% F	5.8-10.1
HbA2	13	4.3 – 6.2% A2	5-10

Each sample was tested once in at least one run on one c 513 analyzer.

Results obtained with the Tina-quant Hemoglobin A1cDx Gen.3 assay (Hemolysate Application) on the c 513 analyzer will be compared to those obtained with the reference methods.

For purposes of this experiment, the data was collected using the Hemolysate Application. This is acceptable since variant interference is a matter of specificity of the antibody. Therefore, the data shown is representative of both the whole blood and hemolysate applications.

There was no significance interference with any of the major hemoglobin variants. Results are summarized in the table below.

Hemoglobin Variant Testing Results

Percent Relative Bias from Reference Method at Low and High Concentrations of HbA1c Samples				
	~6.0% HbA1c		~9.0% HbA1c	
Hb Variant	Relative % Difference	Range	Relative % Difference	Range
HbA2	-2.0%	-3.5 - (-1.3)	1.2%	-1.2 - 2.5
HbC	-1.3%	-4.0 - 1.79	-1.3%	-4.79 - 2.45
HbD	-1.5%	-1.9 - 0.8	-2.3%	-2.4 - (-0.3)
HbE	-1.8%	-4.5 - (-0.2)	0.7%	-0.9 - 2.5
HbS	-1.6%	-4.1 – 3.4	2.7%	-0.3 – 3.0
HbF	Specimens containing high amounts of HbF (> 7 %) may yield lower than expected HbA1c values.			

Heterozygous presence of the most common hemoglobin variants (HbAS, HbAC, HbAD, HbAE) does not interfere. Significant interference was defined as ≥7% change in HbA1c value in the presence of the hemoglobin variant relative to control.

5. CONCLUSIONS

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