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

A. 510(k) Number:

k180509

B. Purpose for Submission:

New Device

C. Measurand:

Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Quantitative, boronate fluorescence quenching

E. Applicant:

EKF Diagnostic GmbH

F. Proprietary and Established Names:

Quo-Test A1c System

G. Regulatory Information:

Product Code	Regulation Name	Classification	Regulation Section	Panel
LCP	Glycosylated Hemoglobin Assay	Class II	21 CFR 864.7470	Hematology (81)
JJE	Discrete photometric chemistry analyzer for clinical use	Class I	21 CFR 862.2160	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Quo-Test A1c System is intended for the in vitro quantitative determination of glycated hemoglobin (%HbA1c) levels in venous whole blood samples (using K2EDTA and lithium heparin anticoagulants).

   Measurement of percent glycated hemoglobin (%HbA1c) is effective for monitoring long-term glycemic control in individuals previously diagnosed with diabetes mellitus.

   The Quo-Test A1c System is not intended for screening or diagnosis of diabetes or neonatal use. The device is intended for professional use in a clinical laboratory setting.

3. Special conditions for use statement(s):

   For prescription use only.

   The Quo-Test A1c System is not intended for point-of-care use.

   This test should not be used for analyzing samples from patients with conditions causing shortened red blood cell survival, such as hemolytic diseases, pregnancy and significant acute or chronic blood loss.

   The test is not intended for judging day- to-day glucose control and should not be used to replace daily home testing of urine or blood glucose.

   For hemoglobin concentrations outside of the range of 6.5 g/dl to 20.4 g/dl (4.0 mmol/l to 12.7 mmol/l) or for HbA1c values outside the range of 4.0 % to 15.0 % HbA1c, a result will not be reported and an error message will be displayed.

   For samples containing the hemoglobin variant HbAE, a positive bias interference of 9.2% has been observed; values could be falsely elevated by up to 0.51% HbA1c.

4. Special instrument requirements:

   Quo-Test Analyzer

I. Device Description:

The Quo-Test A1c System, comprised of the Quo-Test Analyzer and Quo-Test A1c Test Kit, are intended for the in-vitro quantitative determination of glycated hemoglobin in venous whole blood for clinical laboratory testing. The system contains a fluorimeter and two photometers to enable both fluorescent and photometric measurements to be made. The Quo-Test A1c System is calibrated by the manufacturer. There are no user-serviceable parts in the Quo-Test Analyzer. It has ports to support a printer and barcode scanner plus a USB port. It is powered by an AC/DC adapter plugged into a 100-240V AC outlet. The Quo-Test A1c Test Kit contains Quo-Test Blood Collectors (treated with EDTA and surfactant) and Quo-Test A1c Test Cartridges, which contain a plastic vial with ammonium chloride buffer, lysis agent, sodium azide), and a boronate fluorophore conjugate. Each test cartridge is for single-use. The test cartridges are supplied in individual foil pouches and should be stored at 2 - 8°C.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Alere Afinion HbA1c
   Alere Afinion AS100 Analyzer

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

   k151809

3. Comparison with predicate:

Similarities and Differences		
Item	Quo-Test A1c System (Candidate Device)	Alere Afinion HbA1c on Alere Afinion AS100 Analyzer k151809 (Predicate Device)
Intended Use	The Quo-Test A1c System is intended for the in vitro quantitative determination of glycated hemoglobin (%HbA1c) levels in whole blood samples for monitoring long-term glycemic control	Same
Specimen Type	K_2EDTA or lithium heparin venous whole blood	Fingerstick capillary and K_2EDTA, heparin citrate or NaF venous whole blood

Similarities and Differences		
Item	Quo-Test A1c System (Candidate Device)	Alere Afinion HbA1c on Alere Afinion AS100 Analyzer k151809 (Predicate Device)
Testing Environment	Professional use	Professional and Point-of-Care use
Methodology	Boronate fluorescence quenching	Boronate affinity
Measuring Range	4-15%	Same

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

Clinical and Laboratory Standards Institute (CLSI) EP05-A3: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Third Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

CLSI EP07-A2: Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition

CLSI EP25-A, Evaluation Of Stability Of In Vitro Diagnostic Reagents; Approved Guideline

CLSI H15-A3, Reference and Selected Procedure for the Quantitative Determination of Hemoglobin in Blood

CLSI H26-A2, Validation, Verification and Quality Assurance of Automated Hematology Analyzers

IEC 61010-1 Edition 3.0 2010-06, Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements [including: corrigendum 1 (2011)]

L. Test Principle:

The Quo-Test A1c System uses a boronic acid–fluorophore conjugate as the active ingredient for the detection of A1c in a blood sample and the Quo-Test Analyzer uses two measurements of fluorescence to calculate the percentage A1c in the sample. The first measurement is used to calculate the total concentration of hemoglobin in the sample. When the operator places a test cartridge into the analyzer, the dried reagent is automatically added to the assay buffer and re-suspended. The analyzer then measures

the baseline level of fluorescence in the assay buffer. Following this the analyzer then automatically adds the blood sample and the fluorescence is measured immediately. The decrease in measured fluorescence between pre-and post-blood addition is a function of the concentration of the total hemoglobin in the sample.

The second fluorescence measurement is used to calculate the amount of A1c in the sample. The analyzer measures the fluorescence over a 180 second period. As the boronic acid–fluorophore conjugate binds to the A1c in the sample, the fluorescence is quenched due to the proximity of the hemoglobin protein with the fluorophore. This gradual quenching of the fluorescence is a function of the concentration of A1c in the sample. An algorithm then uses the two measurements to calculate the percentage A1c in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   An internal precision study for the Quo-Test A1c System was performed based on CLSI EP05-A3 using three K_2EDTA venous whole blood samples (~5 %, ~8%, and ~10% HbA1c) and two controls (normal, ~6.75%, and abnormal, ~11%). Samples were analyzed using three Quo-Test Analyzers and three lots of Quo-Test A1c Test Kit reagents. Each sample was analyzed in duplicate in two runs per day for 20 days.

Analyzer and Cartridge lot	Sample	%HbA1c (mean)		Within Run	Between Run	Between Day	Total
A	Low	5.26	SD	0.07	0.03	0.03	0.08
			%CV	1.34	0.64	0.48	1.56
	Medium	8.20	SD	0.09	0.03	0.09	0.13
			%CV	1.09	0.31	1.04	1.54
	High	10.39	SD	0.12	0.07	0.08	0.16
			%CV	1.16	0.63	0.82	1.55
	Normal Control	6.95	SD	0.07	0.00	0.02	0.07
			%CV	1.00	0.00	0.30	1.00
	Abnormal Control	11.03	SD	0.10	0.04	0.05	0.12
			%CV	0.95	0.34	0.46	1.11
B	Low	5.08	SD	0.07	0.05	0.03	0.09
			%CV	1.39	0.96	0.59	1.79

Analyzer and Cartridge lot	Sample	%HbA1c (mean)		Within Run	Between Run	Between Day	Total
	Medium	8.09	SD	0.10	0.03	0.07	0.13
			%CV	1.22	0.34	0.90	1.55
	High	10.32	SD	0.09	0.07	0.08	0.14
			%CV	0.87	0.68	0.81	1.37
	Normal Control	6.75	SD	0.06	0.00	0.04	0.07
			%CV	0.94	0.00	0.55	1.06
	Abnormal Control	10.96	SD	0.10	0.05	0.02	0.12
			%CV	0.93	0.47	0.22	1.06
C	Low	5.00	SD	0.07	0.02	0.04	0.08
			%CV	1.31	0.45	0.87	1.63
	Medium	8.01	SD	0.09	0.05	0.06	0.12
			%CV	1.07	0.01	0.78	1.46
	High	10.19	SD	0.08	0.06	0.06	0.12
			%CV	0.78	0.62	0.58	1.15
	Normal Control	6.59	SD	0.08	0.03	0.03	0.09
			%CV	1.16	0.42	0.48	1.33
	Abnormal Control	10.77	SD	0.06	0.08	0.05	0.11
			%CV	0.60	0.70	0.46	1.03

b. Linearity/assay reportable range:

The linearity of the Quo-Test A1c System was evaluated based on CLSI EP06-A. K_2-EDTA venous whole blood samples with a high level (15.2%) and a low-level (4.8%) HbA1c were mixed in different proportions to generate a series of 11 concentrations that were each measured in replicates of five. Linear regression analysis of measured values versus expected values was conducted for each of three cartridge lots. The results of this analysis are shown below:

Lot	Slope	Intercept	R^2
1	0.9981	0.1427	0.999
2	0.9872	0.1983	0.999
3	1.0011	0.0529	1.000

This linearity study supports the Quo-Test A1c System claimed measuring range of 4.0 to 15%.

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

The Quo-Test A1c System reports values in % hemoglobin A1c traceable to the IFCC reference method and traceable to DCCT/NGSP by calculation. The Quo-Test A1c System is certified with the National Glycohemoglobin Standardization Program (NGSP). The certification expires in one year. See the NGSP website for current certification at http://www.ngsp.org.

d. *Detection limit:*

The claimed measuring range of 4.0 to 15% for the Quo-Test A1c System is based on linearity; see section M.1.b.

e. *Analytical specificity:*

Interference studies were performed to assess common or known endogenous and exogenous substances that could interfere with the Quo-Test A1c System. The interfering substances were evaluated in three venous whole blood K_2EDTA samples with ~5%, ~7.5%, and ~10.3% HbA1c. Test samples were prepared by spiking each potential interferent listed below at a single dose into each HbA1c sample. Test samples were assayed in replicates of five and the mean concentration for each test sample was compared to the mean concentration of five replicates of the control sample. The sponsor defined significant interference as greater than or equal to 6% relative deviation between the test and control sample.

The highest concentration of endogenous substances tested that show non-significant interference are summarized in the table below:

Potential interfering substance	Highest concentration tested without significant interference
Ascorbic Acid	3 mg/dL
Bilirubin, unconjugated	20 mg/dL
Bilirubin, conjugated	30 mg/dL
Creatinine	30 mg/dL
Rheumatoid factor IgA	200 IU/mL
Rheumatoid factor IgG	80 IU/mL
Rheumatoid factor IgM	200 IU/mL
Triglycerides	1500 mg/dL
Cholesterol	500 mg/dL
Glucose	1000 mg/dL
Uric acid	20 mg/dL
Acetaminophen	20 mg/dL
Caffeine	30 mg/dL
Dopamine	13 mg/dL
Glybenclamide	20 mg/dL

Potential interfering substance	Highest concentration tested without significant interference
Hydroxyzine dihydrochloride	30 mg/dL
Ibuprofen	40 mg/dL
Metformin	5.1 mg/dL
Acetylsalicylic Acid	50 mg/dL
Salicylic Acid	50 mg/dL
Tetracycline	4 mg/dL
Tolazamide	100 mg/dL
Tolbutamide	100 mg/dL

Hemoglobin Derivatives

No significant interference, defined as greater than or equal to 6% relative deviation between the test and control sample, was observed with carbamylated hemoglobin (up to 12.9%) o labile glycated hemoglobin.

Hemoglobin variant interference

Hemoglobin variant testing was conducted to determine if there is significant interference with the major hemoglobin variants and the Quo-Test A1c System. The study was performed using a total of 32 whole blood samples with the variants evaluated as follows:

Hemoglobin Variant	Number of Samples	Hemoglobin Variant Range (%)	%HbA1c Range
HbA2	4	4.4-5.7	5-7.4
HbC	4	32-34	5.0-11.6
HbD	4	40-41	5.0-9.0
HbE	4	20-26	5.9-9.2
HbF	8	3.2-11	6.5-8.1
HbJ	4	50-51	4.6-11.0
HbS	4	36-40	5.2-10.8

HbA1c test results obtained with the Quo-Test A1c System were compared to HbA1c values assigned to each sample by an FDA-cleared device free of interference with the respective hemoglobin variant. The sponsor calculated the bias between the candidate test result and the assigned value for each sample and defined no significant interference as ≤ ±6% average deviation from the assigned value for all samples containing the same hemoglobin variant.

Testing results indicate that there is no significant interference for HbS (≤ 40%), HbC (≤ 34%), HbD (≤ 41%), HbJ (≤ 51%), and HbA2 (≤ 5.7%). Samples containing high amounts of HbF (> 11%) may result in lower than expected % HbA1c values. HbE concentrations > 20% interfere with this device.

The labeling contains the following information regarding hemoglobin variant interference:

For samples containing the hemoglobin variant HbAE at concentrations >20 %, a positive bias interference of up to 9.2% has been observed, HbA1c values could be falsely elevated by up to 0.51% HbA1c.

The Quo-Test A1c System was found to be unaffected by labile glycated hemoglobin, carbamylated hemoglobin and the following hemoglobin variants:

HbAS (≤ 40 % S), HbAC (≤ 34 % C), HbAD (≤ 41 % D), HbAJ (≤ 51 % J), ß-thalassemia (≤ 5.7 % A2) and elevated fetal hemoglobin (≤ 11 % F). In samples with HbF above 11% an increasing negative bias is observed: HbA1c values could be lower than expected. In samples with HbAE concentrations > 20% interference with this device; HbA1c values could be falsely elevated.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison of the Quo-test A1c System was performed at three sites. K_2-EDTA venous whole blood (n=423) from prospective blood sampling were measured on the Quo-Test A1c System in singlicate and compared to matched venous K_2-EDTA whole blood measured on the Tosoh G8 HPLC Analyzer at a NGSP secondary reference laboratory. The range tested was 4.5-14.6% HbA1c. Each site utilized one Quo-Test A1c Analyzer with three or four study operators at each site. Each site received a different lot of the Quo-Test A1c Test Kit reagents. Linear regression analysis results in NGSP units (%HbA1c) are listed in the tables below.

K_2-EDTA

Site	N	Slope	Intercept	r^2
1	149	0.962	0.070	0.993
2	118	0.969	0.044	0.988
3	156	0.960	0.143	0.993
Overall	423	0.964	0.084	0.993

b. Matrix comparison:

A matrix study was performed using 149 matched, native K_2-EDTA venous whole blood (reference) and lithium heparin venous whole blood samples ranging from 4.9 to 13.3% HbA1c. Samples were collected and tested in singlicate with one reagent

lot on one Quo-Test A1c Analyzer. The linear regression results are shown in the table below:

N	Slope	Intercept	r^2
149	0.996	0.041	0.994

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):

   Not applicable.

4. Clinical cut-off:

   Not applicable.

5. Expected values/Reference range:

   The labeling states the following for those previously diagnosed with diabetes:

   A reasonable A1C goal for many nonpregnant adults is 7% (53 mmol/mol). Providers might reasonably suggest more stringent A1C goals (such as 6.5% [48 mmol/mol]) for selected individual patients if this can be achieved without significant hypoglycemia or other adverse effects of treatment (i.e. polypharmacy). Appropriate patients might include those with short duration of diabetes, type 2 diabetes treated with lifestyle or metformin only, long life expectancy, or no significant cardiovascular disease. Less stringent A1C goals (such as 8% [64 mmol/mol]) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes in whom the goal is difficult to achieve despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin(1).

   (1) American Diabetes Association. Standards of medical care in diabetes - 2018. Diabetes Care. 2018;41 (Suppl 1):S55–S64.

N. Instrument Name:

Quo-Test A1c Analyzer

O. System Descriptions:

1. Modes of Operation:

   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 _____

3. Specimen Identification:

   There is no specimen identification function for this device. The system contains a barcode scanner that can be used optionally to scan operator and patient identity barcodes used for optional labeling of results.

4. Specimen Sampling and Handling:

   Blood is collected using the blood collector which is then inserted into the test cartridge. To collect venous whole blood using the blood collector, the blood must first be transferred onto a clean, non-metallic and non-absorbant surface. The blood collector should not be placed directly into the blood collection tube. The cartridge containing the blood collector is then placed into the receptacle in the analyzer and when the door is closed, the analyzer starts the test.

5. Calibration:

   The Quo-Test A1c Analyzer is factory calibrated and is not adjustable by the user.

6. Quality Control:

   The Quo-Test A1c System should be used with the Quo-Test A1c Control Kit that is available for purchase separately. The Quo-Test A1c Control Kit is a two-level, lyophilized control consisting of human blood, preservatives and stabilizers, one level in the region of a normal patient response (4 - 7% A1c) and one level in the region of an abnormally high patient sample (~10% A1c). A dropper bottle containing distilled water to reconstitute the controls is also provided. Users are directed to perform control testing with each new lot of test cartridges, with each new shipment of test cartridges, and if there is a concern that the result may be incorrect.

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

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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