510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k180296

B. Purpose for Submission:

Addition of a diagnostic claim to an existing device

C. Measurand:

Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Quantitative boronate affinity assay

E. Applicant:

Alere Technologies AS

F. Proprietary and Established Names:

Afinion HbA1c Dx

G. Regulatory Information:

Description	Classification	Regulation	Product Code	Panel
Hemoglobin A1c Test System	Class II	21 CFR 862.1373	PDJ	Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Afinion HbA1c Dx is an *in vitro* diagnostic test for quantitative determination of glycated hemoglobin (% hemoglobin A1c, HbA1c) in human venous and capillary whole blood. This test is to be used as an aid in the diagnosis of diabetes and as an aid in

identifying patients who may be at risk for developing diabetes. The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.

3. Special conditions for use statement(s):

   For prescription use only.

   For in vitro diagnostic use.

   This device has significant negative interference with fetal hemoglobin (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF including those with known Heredity Persistence of Fetal Hemoglobin.

   This test should not be used to diagnose:

   - Diabetes during pregnancy
   - Patients with an elevated fetal hemoglobin (HbF > 10%) such as hereditary persistence of fetal hemoglobin (HPFH)
   - Patients with a hemoglobinopathy but normal red cell turnover (e.g. sickle cell trait)
   - Patients with abnormal red cell turnover (e.g. anemias from hemolysis and iron deficiency)
   - Patients with iron deficiency and hemolytic anemia, various hemoglobinopathies, thalassemias, hereditary spherocytosis, malignancies, and severe chronic hepatic and renal disease
   - Patients that have received a blood transfusion within the past 3 weeks
   - Patients that have received cancer chemotherapy within the past 3 weeks

   In cases of rapidly evolving type 1 diabetes the increase of HbA1c values might be delayed compared to the acute increase in glucose concentrations. In these conditions diabetes mellitus must be diagnosed based on plasma glucose concentration and/or the typical clinical symptoms.

   HbA1c testing should not replace glucose testing for type 1diabetes, in pediatric patients and in pregnant women.

   Coagulated or hemolyzed samples cannot be used with Afinion HbA1c Dx. Samples with > 14% hemolysis (2000 mg/dL) may return an information code.

   If the sample has a hemoglobin value below 6 g/dL or above 20 g/dL, no test result will be reported and an information code will be displayed.

4. Special instrument requirements:

   Afinion AS100 analyzer

I. Device Description:

The Afinion HbA1c Dx is a fully automated boronate affinity assay for the determination of the percentage of hemoglobin A1c in human venous and capillary whole blood. Each assay cartridge contains blue boronic acid conjugate, a tube with a polyethersulfone membrane, and washing solution (morpholine buffered sodium chloride solution with detergents and preservative). Each cartridge is labeled with a unique barcode.

The Afinion HbA1c Dx is factory calibrated and intended for use with the previously cleared Afinion AS100 Analyzer (k050574, k110056) and Afinion HbA1c Controls (k050574).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche Diagnostics Cobas C501 Tina-Quant HbA1c cDx Gen 3 assay

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

   k121610

3. Comparison with predicate:

Similarities		
Item	**Candidate Device Afinion HbA1c Dx**	**Predicate Cobas c 501 Tina-Quant HbA1c Dx Gen. 3 assay (k121610)**
Intended Use	Quantitative determination of hemoglobin A1c for the diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes	Same
Units of measurement	% HbA1c (DCCT/NGSP)	Same
Storage requirements	2-8°C until expiration date	Same
Controls	Provided by manufacturer	Same
Traceability	Traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and Diabetes Control and Complications Trial (DCCT) reference method. Certified via the National Glycohemoglobin	Same

Similarities		
Item	**Candidate Device Afinion HbA1c Dx**	**Predicate Cobas c 501 Tina-Quant HbA1c Dx Gen. 3 assay (k121610)**
	Standardization Program (NGSP)	

Differences		
Item	**Candidate Device Afinion HbA1c Dx**	**Predicate Cobas c 501 Tina-Quant HbA1c Dx Gen. 3 assay (k121610)**
Intended use sites	For use by health care professionals in clinical laboratories and point of care settings	For use by health care professionals in clinical laboratories
Assay principle	Boronate affinity assay. Hemoglobin determination by reflectance measurements of blue conjugate of glycated hemoglobin and red total hemoglobin.	HbA1c determination by turbidimetric inhibition immunoassay method. Hemoglobin determination by converting to a derivative with a characteristic absorption spectrum which is measured bichromatically.
Sample types	Anticoagulated venous whole blood (K_2-EDTA), and capillary whole blood (fingerstick)	Anticoagulated venous whole blood (K_2-EDTA, K_3-EDTA, Li-Heparin, Na-Heparin, NaF/Na_2-EDTA, NaF/K-oxalate, KF/ Na_2-EDTA)
Analyzer	Alere Afinion AS100	Cobas c 501
Calibrators	Factory calibrated, no user calibration required	User calibration using calibrators provided by manufacturer
Assay range	4.00 – 15.00 % HbA1c	4.2 – 20.1 % HbA1c

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

Clinical and Laboratory Standards Institute (CLSI) EP5-A3 Evaluation of Precision Performance of Quantitative Measurement Methods, Approved Guideline—Third Edition.

CLSI EP7-A2 Interference Testing in Clinical Chemistry, Approved Guideline –- Second Edition

CLSI EP5-A3 Evaluation of Precision of Quantitative Measurement Procedures- Approved Guideline –Third Edition

ISO 14971 Second edition 2007-03-01, Medical devices - application of risk management to medical devices

EN ISO 14971:2012 Medical devices, Application of risk management to medical devices

L. Test Principle:

A blood sample is collected with the integrated sampling device, which is then inserted into the Alere HbA1c Dx test cartridge. The cartridge/sampling device combination is then placed into the cartridge chamber of the Alere Afinion AS100 Analyzer. The sample is automatically diluted and mixed with a solution that releases hemoglobin from the erythrocytes. After the hemoglobin is precipitated, the sample mixture is transferred to a blue boronic acid conjugate which binds to the cis-diols of glycated hemoglobin. This reaction mixture is soaked through a filter membrane and all precipitated hemoglobin, conjugate-bound and unbound (i.e. glycated and nonglycated hemoglobin) remains on the membrane. Excess conjugate is removed with a washing reagent. The analyzer measures the reflectance of the precipitate on the membrane as blue (glycated hemoglobin) and red (total hemoglobin) color intensities. The analyzer calculates a ratio proportional to the percentage of HbA1c in the sample and displays as the % HbA1c (DCCT/NGSP).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Internal precision study using venous whole blood
An internal precision study was performed according to CLSI guideline EP05-A3. Four K_2-EDTA venous whole blood samples at concentrations near 5%, 6.5%, 8% and 12% HbA1c were analyzed by eleven operators in duplicate, twice a day, with three lots of reagents, over 20 days each, on nine Afinion AS100 analyzers (three lots per analyzer, three analyzers per sample). For each sample, there were 720 measurements. Results are shown in the tables below:

Analyzer 1 (n = 240):

Level	Mean %HbA1c	Repeatability		Between run		Between day		Between lot		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.13	0.067	1.31	0.017	0.33	0.029	0.56	0.037	0.72	0.084	1.63
Threshold	6.53	0.086	1.31	0.000	0.00	0.039	0.60	0.064	0.98	0.114	1.74
Medium	8.09	0.082	1.01	0.000	0.00	0.045	0.56	0.019	0.23	0.095	1.17
High	11.33	0.100	0.88	0.000	0.00	0.035	0.31	0.105	0.93	0.149	1.32

Analyzer 2 (n = 240):

Level	Mean	Repeatability		Between run		Between day		Between lot		Total	
	%HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.11	0.061	1.19	0.000	0.00	0.034	0.67	0.046	0.89	0.084	1.63
Threshold	6.53	0.070	1.07	0.019	0.30	0.044	0.67	0.064	0.98	0.106	1.62
Medium	8.01	0.060	0.75	0.010	0.13	0.038	0.48	0.042	0.52	0.083	1.04
High	11.17	0.086	0.77	0.015	0.13	0.060	0.54	0.094	0.84	0.142	1.27

Analyzer 3 (n = 240):

Level	Mean	Repeatability		Between run		Between day		Between lot		Total	
	%HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.18	0.053	1.02	0.007	0.14	0.030	0.58	0.041	0.79	0.074	1.43
Threshold	6.58	0.066	1.00	0.000	0.00	0.038	0.58	0.035	0.53	0.084	1.27
Medium	8.08	0.086	1.06	0.035	0.43	0.052	0.64	0.047	0.58	0.116	1.43
High	11.30	0.114	1.00	0.023	0.21	0.031	0.28	0.098	0.87	0.155	1.37

All analyzers combined (n =720):

Level	Mean	Repeatability		Between run		Between day		Between lot		Between analyzer		Total	
	%HbA1	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.14	0.061	1.18	0.000	0.00	0.031	0.60	0.041	0.81	0.030	0.58	0.08	1.64
Threshold	6.55	0.074	1.13	0.000	0.00	0.040	0.62	0.056	0.85	0.000	0.00	0.09	1.51
Medium	8.06	0.077	0.95	0.016	0.20	0.045	0.56	0.038	0.47	0.039	0.49	0.10	1.31
High	11.26	0.101	0.89	0.014	0.12	0.044	0.39	0.099	0.88	0.059	0.52	0.16	1.42

External precision study using venous whole blood

An external precision study was performed at three point-of-care moderate complexity laboratory sites in the US. Four K_2-EDTA venous whole blood samples at concentrations near 5%, 6.5%, 8% and 12% HbA1c were analyzed by two to three operators per site using six Afinion AS100 analyzers and three lots of reagent. Four replicates were analyzed twice a day for 10 days for a total of 240 measurements per sample at each site. The data was analyzed according to CLSI EP05-A3 and results are shown in the table below:

All sites combined:

Level	Mean	Repeatability		Between run		Between day		Between lot		Between analyzer		Total	
	%HbA1	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.02	0.061	1.21	0.029	0.57	0.02	0.44	0.046	0.92	0.030	0.58	0.085	1.78
Threshold	6.41	0.071	1.11	0.030	0.48	0.02	0.40	0.047	0.74	0.000	0.00	0.095	1.48
Medium	8.18	0.090	1.10	0.019	0.23	0.02	0.28	0.042	0.51	0.039	0.49	0.104	1.36
High	12.09	0.118	0.97	0.046	0.38	0.03	0.25	0.033	0.27	0.059	0.52	0.134	1.22

Capillary blood (fingerstick) precision:

Capillary blood (fingerstick) precision estimates are based on a combination of three separate studies as described below:

i. Capillary blood (fingerstick) precision estimates for repeatability and between-lot were calculated from measurements obtained during the method comparison study. Ten intended use operators analyzed duplicate fingerstick samples from 170 subjects with three reagent lots in total (two lots per site) on five Afinion AS100 analyzers at three sites. The samples were grouped into four %HbA1c concentration intervals (4.00-5.99, 6.00-6.99, 7.00-9.99, 10.00-15.00) and analyzed according to CLSI guideline EP05-A3. Results are presented in the table below:

Level	N	Minimum %HbA1c	Maximum %HbA1c	Average %HbA1c	Repeatability		Between lot		Total	
					SD	%CV	SD	%CV	SD	%CV
Low	45	4.77	5.99	5.42	0.082	1.52	0.065	1.20	0.105	1.93
Threshold	68	6.00	6.98	6.46	0.088	1.36	0.027	0.42	0.092	1.42
Medium	51	7.02	9.94	7.93	0.107	1.35	0.000	0.00	0.107	1.35
High	6	10.07	11.52	10.72	0.067	0.62	0.008	0.07	0.067	0.62

ii. To capture repeatability, between-instrument, and between-operator precision estimates, an external study was performed at three point-of-care moderate complexity laboratory sites in the US. Samples in four %HbA1c concentration intervals (4.00-5.99, 6.00-6.99, 7.00-9.99, 10.00-15.00) from five or six subjects per interval were analyzed by three operators per site using two Afinion AS100 analyzers. Six fingerstick samples (two fingerstick samples from each subject were collected and measured per operator) were analyzed for a total of 30 or 36 measurements (M) per sample level at each site (n=90 or n=96 measurements across sites). The results from all sites combined are shown in the table below.

Level	N (M)	Average %HbA1c	Repeatability		Between Instrument		Between Operator		Total	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	15 (90)	5.33	0.074	1.39	0.008	0.14	0.00	0.00	0.075	1.40
Threshold	15 (90)	6.51	0.081	1.25	0.019	0.30	0.00	0.00	0.083	1.28
Medium	16 (96)	8.32	0.092	1.10	0.000	0.00	0.017	0.21	0.093	1.12
High	15 (90)	12.20	0.139	1.14	0.057	0.47	0.00	0.00	0.150	1.23

iii. Between-Run and Between-Day precision estimates for capillary blood were transferred from the internal venous whole blood precision study described above.

The combined precision estimates (%CV) from the three studies are shown in the table below.

Level	Fingerstick Accuracy Precision		Internal Venous Precision Study		Fingerstick Precision Study			Total %CV
	Repeatability	Between Lot	Between Run	Between Day	Repeatability	Between Instrument	Between Operator	
Low	1.52	1.2	0.00	0.60	-	0.14	0.00	2.03
Threshold	1.36	0.42	0.00	0.62	-	0.30	0.00	1.58
Medium	1.35	0	0.20	0.56	-	0.00	0.21	1.49
*High	-	0.07	0.12	0.39	1.14	0.47	0.00	1.30

*This estimate of the Total %CV for High HbA1c (≥ 10%) is based on the within run component of variance estimated in the Fingerstick Precision Study since the precision study has a larger sample size than the Fingerstick Accuracy Precision Study.

b. *Linearity/assay reportable range:*

Linearity was previously established for the range of 4.00 – 15.00 % HbA1c (DCCT/NGSP) in k050574.

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

The Afinion HbA1c Dx assay is certified with the National Glycohemoglobin Standardization Program (NGSP). The NGSP certification expires in one year. See NGSP website for current certification at http://www.ngsp.org. Traceability is verified annually through the IFCC Whole Blood Monitoring Program.

Test results are calculated in mmol/mol (IFCC). HbA1c values are further reported according to the National Glycohemoglobin Standardization Program (NGSP) recommendations at DCCT (Diabetes Control and Complications Trial) level. The IFCC Master Equation for the relationship between the IFCC-Reference Method (RM) and the NGSP-Designated Comparison Method (DCM) is used for conversion of the test results:

NGSP-HbA1c (%) = DCCT-HbA1c (%) = 0.09148 x IFCC-HbA1c (mmol/mol) + 2.152

d. *Detection limit:*

The Limit of Quantification was previously established as 4.0% HbA1c in k050574.

e. *Analytical specificity:*

i. Exogenous and endogenous interference

Interference from 20 drug substances and six endogenous compounds was evaluated using K_2-EDTA venous whole blood samples with low (~6.5%) and high (≥ 8.5%) HbA1c levels. Test samples were prepared by spiking each drug or endogenous substance into the low and high samples and comparing to control

samples containing no drug. The test and control samples were tested in 10 replicates using two lots of reagent. The sponsor defined significant interference as greater than or equal to 7% difference from the expected concentration. Results demonstrated that no significant interference was observed with the following substances up to the listed concentrations:

Substance	Highest concentration tested with no significant interference
Acetaminophen	20 mg/dL
Acetylcysteine	166 mg/dL
Acetylsalicylic acid	100 mg/dL
Ampicillin	100 mg/dL
Ascorbic acid	30 mg/dL
Bilirubin –conjugated	60 mg/dL
Bilirubin - unconjugated	60 mg/dL
Cefoxitin	250 mg/dL
Cyclosporine A	0.5 mg/dL
Cyclosporine C	0.5 mg/dL
Doxycyclin	5 mg/dL
Glucose	1000 mg/dL
Glyburide	0.20 mg/dL
Heparin	5000 U/L
Ibuprofen	50 mg/dL
Intralipid	1000 mg/dL
Levodopa	2 mg/dL
Metformin	4 mg/dL
Methyldopa	2 mg/dL
Metronidazole	20 mg/dL
Phenylbutazone	40 mg/dL
Rheumatoid factor	780 000 IU/L
Rifampicin	6.4 mg/dL
Salicylic acid	59 mg/dL
Theophylline	10 mg/dL
Total protein (human serum albumin added and native total	150 g/L

Potential interference from hemolysis was evaluated using two K_2-EDTA venous whole blood samples at 6.5% and ~9.5% HbA1c. Test samples were spiked with hemolysates generated by a freeze/thaw cycle of native samples and compared to control samples containing no hemolysate. The sponsor defined significant interference as greater than or equal to 7% difference from the expected

concentration. The results support the sponsor's claim that hemolysis up to 13.8% does not interfere with their device. The labeling states that "hemolyzed samples with > 14% hemolysis (2000 mg/dL) may return an information code.".

ii. Cross reactivity with Hemoglobin Derivatives

Potential cross reactivity with acetylated hemoglobin, carbamylated hemoglobin, labile HbA1c, and glycated albumin was evaluated. Two K_2-EDTA venous whole blood samples at 6.5% and ~8.5% HbA1c were spiked with the potential interferent (6.0 mg/mL acetylated hemoglobin, 14.1 mg/mL carbamylated hemoglobin, 12.4 mg/mL labile HbA1c, 7.7 mg/mL glycated albumin). Ten replicates of test and control samples were analyzed. The sponsor defined significant interference as greater than or equal to 7% difference from the expected concentration. The testing results support the sponsor's claim in the labeling that there is no cross reactivity with acetylated hemoglobin (4.6 mg/mL), carbamylated hemoglobin (13.8 mg/mL), labile HbA1c (11.4 mg/mL), or glycated albumin (7.7 mg/mL).

Potential cross reactivity from HbA0, HbA1a and HbA1b was evaluated using 100 samples. Two HbA1c concentrations of pooled K_2-EDTA venous whole blood samples at 6.0% and 9.0% HbA1c (range 4.3% to 13.93% HbA1c) containing HbA0 (82% to 95%), HbA1a (0.4% to 1.4%) and HbA1b (0.4% to 2.3%) were tested in singlicate using an Afinion AS100 analyzer and compared to measurements made using a NGSP comparator method (Tosoh G8 HPLC). The sponsor defined significant interference as greater than or equal to 7% difference from the expected concentration. The testing results support the sponsor's claim in the labeling that there is no cross reactivity with HbA0 (up to 95%), HbA1a (up to 1.4%), and HbA1b (up to 2.3%).

iii) Hemoglobin Variant Interference

For the hemoglobin variant interference study was performed using a total of 221 K_2-EDTA venous whole blood samples known to contain common hemoglobin variants (HbA2, HbS, HbC, HbE, HbD, and HbF). Results obtained by a FDA cleared method that has been demonstrated to be free from the hemoglobin interference being tested (Premier Hb9210 for HbA2, HbAS, HbE, and Tosoh Automated Glycohemoglobin Analyzer HLC-723 G8 for HbF). The sponsor's definition of non-significant interference is ≤7% mean relative deviation between the Afinion HbA1c Dx result and the NGSP comparator method.

Samples used for interference evaluation:

Hemoglobin Variant	Number of Samples Tested	% Content of Variant in sample	Range in Concentration in % HbA1c
HbA2	26	3.9-5.7	5.8-10.6
HbS	21	35-42	5.6-8.8

Hemoglobin Variant	Number of Samples Tested	% Content of Variant in sample	Range in Concentration in % HbA1c
HbC	25	30-36	5.5-9.7
HbE	20	17-26	6.1-8.9
HbD	21	27-42	6.1-9.4
HbF	121	3.4-28.1	5.0-11.3

Hemoglobin Variant Result Summary:

	Mean % Bias (range of relative bias) from Comparator Method	
Hb Variant	**~6.5 % HbA1c**	**~8.5 % HbA1c**
HbA2	-3.4 % (-6.2% to -1.4%)	-2.5 % (-6.6% to 2.8%)
HbS	-4.1 % (-6.6% to 3.2%)	-1.0 % (-9.9% to 3.5%)
HbC	-5.5 % (-8.5% to -1.8%)	-1.8 % (-5.2% to 1.1%)
HbE	3.5 % (1.4% to 7.9%)	3.7 % (0% to 4.7)
HbD	-2.2 % (-4.1% to 0%)	-2.9 % (-5.9% to 0%)
HbF	10.4% HbF is the highest HbF concentration where no significant interference is observed with significant interference defined as > ±7%.	

The testing results show there is no significant interference for Hemoglobin A2 (≥ 5.7%), Hemoglobin S (≥ 42%), Hemoglobin C (≥ 36%), Hemoglobin E (≥ 26%), and Hemoglobin D (≥ 42%).

The package insert labeling states:

> No significant interference for Hemoglobin A2, Hemoglobin C, Hemoglobin D, Hemoglobin E, and Hemoglobin S up to the levels stated.
>
> The results show that there is significant interference due to the presence of HbF at a HbF concentration of > 10.4%. The device labeling contains the following prominent boxed warning:
>
> > "This device has significant negative interference with fetal hemoglobin (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF including those with known Heredity Persistence of Fetal Hemoglobin. Refer to the Analytical specificity and Limitations sections in this package insert for details."

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study was conducted using 120 capillary (fingerstick) whole blood samples and matched K_2-EDTA venous whole blood samples ranging from 4.6 to 11.4 % HbA1c. All samples were tested with two Afinion HbA1c Dx reagent lots at three moderate complexity point-of-care laboratories. The distribution of samples spanned a concentration around the clinical decision points as follows:

Hemoglobin A1c level	Number of samples	Percent of samples
4 – 5%	5	4.2%
5.1 – 6%	15	12.5%
6.1 – 6.5%	30	25.0%
6.6 – 7%	30	25.0%
7.1 – 8%	20	16.7%
8.1 – 9%	10	8.3%
9.1 – 15%	10	8.3%
Total samples	120	100%

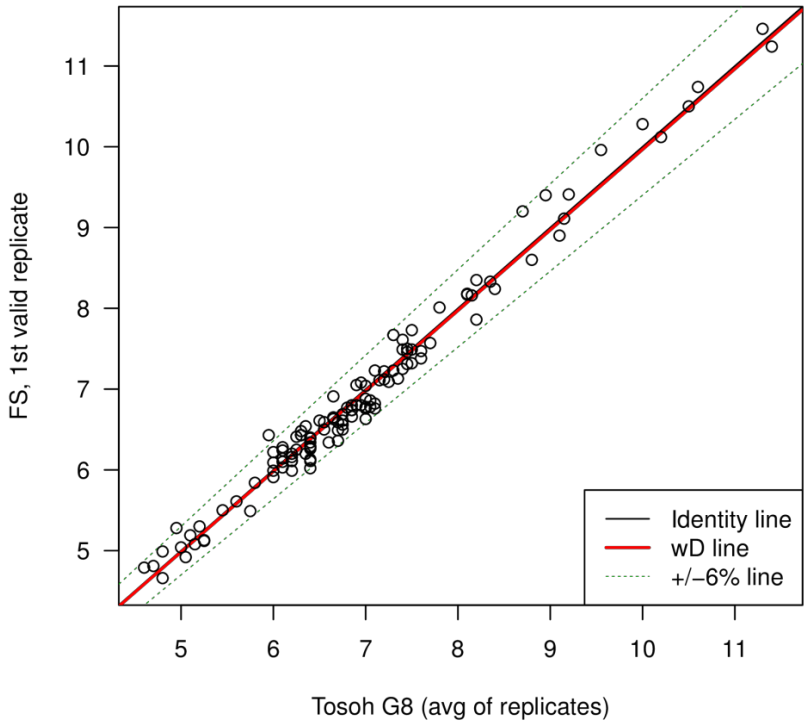
Singlicate capillary and venous whole blood results from the Afinion HbA1c Dx test system were compared to average results from matched K_2-EDTA venous whole blood samples tested in duplicate using a NGSP comparator method (Tosoh G8 HPLC).

Deming (weighted) and Passing-Bablok regression analyses were performed for the Afinion HbA1c Dx assay versus the comparator method.

Fingerstick capillary whole blood samples

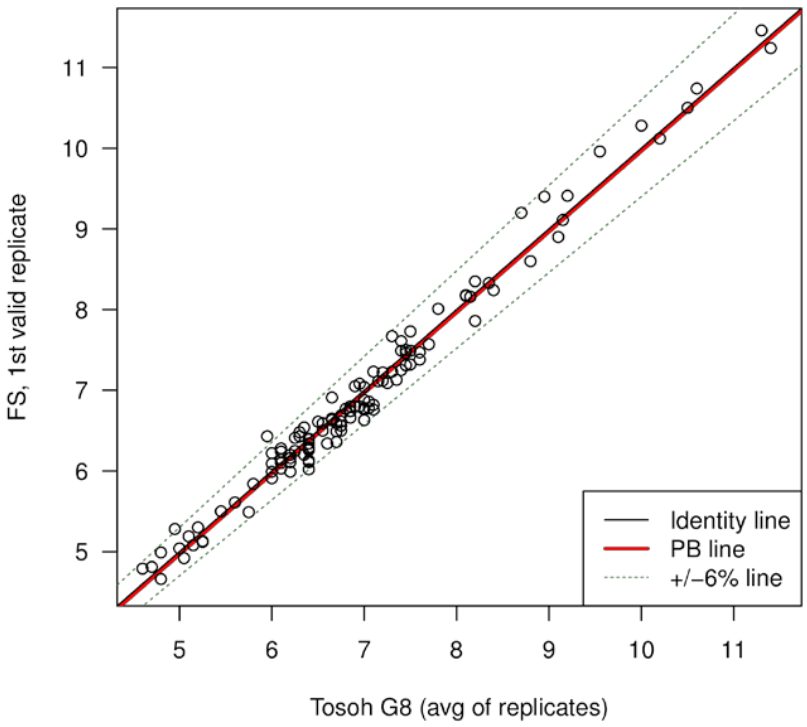
Weighted Deming regression:

y-intercept	Slope	95% CI
0.000	0.997	0.966 – 1.027 (slope) -0.209 – 0.201 (intercept)



Passing-Bablok regression:

y-intercept	Slope	95% CI
-0.040	1.000	0.971 – 1.033 (slope) -0.271 – 0.165 (intercept)



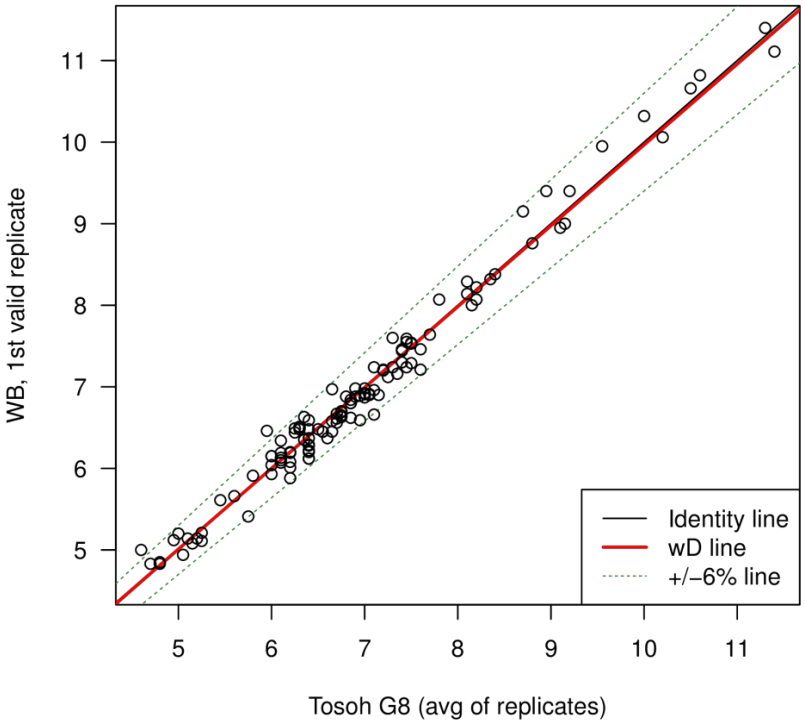
The following biases for fingerstick blood samples were observed between the Afinion HbA1c Dx and the comparator method:

Decision Level	Weighted Deming regression		Passing-Bablok regression	
	Bias	% Bias	Bias	% Bias
5.0%	-0.017	-0.335	-0.040	-0.800
6.5%	-0.022	-0.334	-0.040	-0.615
8.0%	-0.027	-0.334	-0.040	-0.500
12.0%	-0.040	-0.333	-0.040	-0.333

Venous whole blood samples

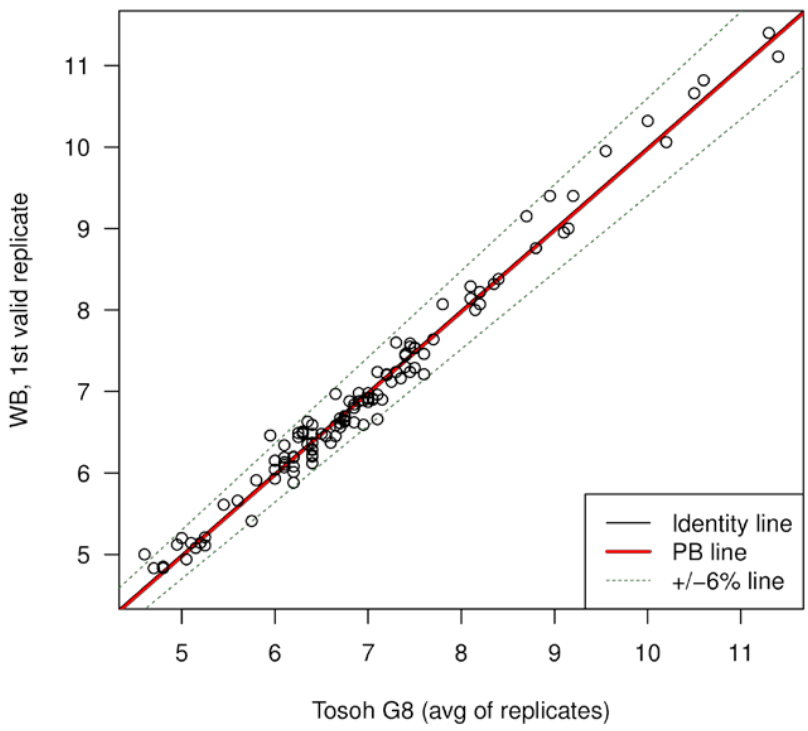
Weighted Deming regression:

y-intercept	Slope	95% CI
0.053	0.991	0.959 – 1.022 (slope) -0.162 – 0.270 (intercept)



Passing-Bablok regression:

y-intercept	Slope	95% CI
-0.030	1.000	0.968 – 1.031 (slope) -0.232 – 0.184 (intercept)



The following biases were observed between the Afinion HbA1c Dx and the comparator method:

Decision Level	Weighted Deming regression		Passing-Bablok regression	
	Bias	% Bias	Bias	% Bias
5.0%	0.010	0.195	-0.030	-0.600
6.5%	-0.003	-0.052	-0.030	-0.462
8.0%	-0.017	-0.206	-0.030	-0.375
12.0%	-0.051	-0.429	-0.030	-0.250

Total Error Calculations

Using the results of bias estimation (% Bias) in the method comparison study and precision estimates, Total Error (TE) at four concentrations (5.0%, 6.5%, 8.0%, and 12.0%) was calculated using all components of variance as stated in the special controls as follows: % TE = |% Bias| + 1.96 *% CV*(1+ % Bias/100). The results are presented in the tables below.

Capillary fingerstick samples:

Level	%CV	Weighted Deming regression		Passing-Bablok regression	
		%Bias	%TE	%Bias	%TE
5.0%	2.03	-0.335	4.30	-0.800	4.75
6.5%	1.58	-0.334	3.42	-0.615	3.69
8.0%	1.49	-0.334	3.24	-0.500	3.40
12.0%	1.30	-0.333	2.87	-0.333	2.87

EDTA venous whole blood samples (based on external point-of-care precision study):

Level	%CV	Weighted Deming regression		Passing-Bablok regression	
		%Bias	%TE	%Bias	%TE
5.0%	1.78	0.195	3.69	-0.600	4.07
6.5%	1.48	-0.052	2.95	-0.462	3.35
8.0%	1.36	-0.206	2.87	-0.375	3.03
12.0%	1.22	-0.429	2.81	-0.250	2.64

EDTA venous whole blood samples (based on internal precision study):

Level	%CV	Weighted Deming regression		Passing-Bablok regression	
		%Bias	%TE	%Bias	%TE
5.0%	1.64	0.195	3.42	-0.600	3.80
6.5%	1.51	-0.052	3.01	-0.462	3.41
8.0%	1.31	-0.206	2.77	-0.375	2.93
12.0%	1.42	-0.429	3.20	-0.250	3.03

b. Matrix comparison:

Not applicable. Venous K_2-EDTA and capillary are the only matrices claimed for this assay.

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**:**

   See expected values, below.

5. Expected values/Reference range:

   The diagnostic cut-off is 6.5 % HbA1c. Patients with HbA1c values in the range 5.7-6.4 % are identified as having an increased risk for developing diabetes[1,2].

   [1]International Expert Committee, International Expert Committee Report on the Role of the A1c Assay in the Diagnosis of Diabetes. Diabetes Care 2009; 32(7):1237-1334.

   [2]American Diabetes Association. Classification and Diagnosis of Diabetes. Diabetes Care 2018; 41(Suppl. 1): S13-S27.

N. Proposed Labeling:

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

O. Conclusion:

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