



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

I Background Information:

A 510(k) Number

K192987

B Applicant

Jana Care, Inc.

C Proprietary and Established Names

Aina HbA1c Monitoring System 2

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LCP	Class II	21 CFR 864.7470 - Glycosylated Hemoglobin Assay	HE - Hematology

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Whole blood glycosylated hemoglobin (HbA1c)

C Type of Test:

Boronate affinity, photometry

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Aina HbA1c Monitoring System 2 consists of the Aina 2 Automated HbA1c Device, the Aina Device, Aina HbA1c Test Kits, mobile device, and the Aina Mobile Application. It is intended to be used for quantitative measurement of %HbA1c (DCCT/NGSP) and mmol/mol HbA1c (IFCC) in human anticoagulated venous whole blood. It is intended for in-vitro diagnostic use by healthcare professionals in a laboratory environment to monitor long term glycemic control of persons previously diagnosed with diabetes. This test is not intended for use in the diagnosis of or screening for diabetes or for use on neonates.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

- For in vitro diagnostic use.
- The Aina HbA1c Monitoring System 2 is not intended for point-of-care use.
- This test should not be used in monitoring daily glucose and should not be used to replace daily home testing of urine and blood glucose levels.
- This test is not intended for use in the diagnosis of or screening for diabetes.
- This test is not intended for use on neonates.
- 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.
- Samples with a hemoglobin concentration lower than 7.2 g/dL or higher than 20 g/dL can cause inaccurate test results.
- “WARNING: The Hemoglobin A1c assay has significant negative interference from Hemoglobin F (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin.”

D Special Instrument Requirements:

The Aina 2 Automated HbA1c Device, the dedicated smartphone with the Aina Mobile Application, and the Aina Device.

IV Device/System Characteristics:

A Device Description:

The system consists of the Aina 2 Automated HbA1c Device for sample processing that connects to a dedicated smartphone with the Aina Mobile Application, the Aina Device for optical test strip readout, Aina HbA1c Test Kits which contain all the reagents necessary for running each

HbA1c test. The smartphone is provided with the device system by the manufacture and has had functionalities that are not needed for running the HbA1c test locked down prior to providing it to customers. The Aina Device is a reflectance based colorimetric sensor device that connects to the mobile device through the audio jack. The smartphone runs the Aina Mobile Application that allows for user interaction and illustrates the step by- step testing process on its touchscreen. Streck A1c-Cellular control solutions can be used for regular quality control checking of the system.

B Principle of Operation:

The Aina HbA1c Test utilizes the boronate affinity method. The Aina HbA1c Test Kit consists of test strips, reagents, wash buffers, capillary tubes for sample collection, and pipette tips. The reagent contains a lysing agent and a blue boronic acid conjugate. When blood is added to the reagent, the erythrocytes are lysed and all hemoglobin precipitates. The boronic acid conjugates binds to the glycosylated hemoglobin. An aliquot of the reaction mixture is applied to the test strip and all the precipitated hemoglobin, conjugate bound and unbound, remains on top of the filter. Any unbound boronate is removed with the wash buffer. The precipitate is evaluated by measuring the blue (glycosylated hemoglobin) and the red (total hemoglobin) color intensity respectively with the Aina Device, the ratio between them being proportional to the percentage of the glycosylated hemoglobin in the sample.

C Instrument Description Information:

Modes of Operation	Yes	No
Does the applicant’s device contain the ability to transmit data to a computer, webserver, or mobile device?	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Does the applicant’s device transmit data to a computer, webserver, or mobile device using wireless transmission?	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Software		
FDA has reviewed applicant’s Hazard Analysis and software development processes for this line of product types.	<input checked="" type="checkbox"/>	<input type="checkbox"/>

1. Instrument Name:

Aina HbA1c Monitoring System 2

2. Specimen Identification:

There is no specimen identification function for this device.

3. Specimen Sampling and Handling:

Venous whole blood is collected in a K2-EDTA vacutainer tube. A drop of blood is placed on a hydrophobic surface, such as parafilm, using a pipette. The capillary tube provided in the test kit is filled with blood and dropped inside the reagent vial which is inserted into along with the test strip. When the Aina Device has finished processing the sample the test strip is removed and inserted into the Aina Device for measurement.

4. Calibration:

Calibration is established for each lot of Test Kit and stored as a 3-digit code. When the code is entered in the Aina Mobile Application by the user, the calibration data for the test kit lot is transferred and used for calculating results.

5. Quality Control:

Streck A1c-Cellular control solutions, 2 levels, are recommended for use for regular quality control checking of the system. Users are directed to perform control testing if repeated unexpected results are obtained, when opening a new test kit, if any issue with the Aina 2 device or any component of the test kit is suspected, or if the Aina 2 device is dropped.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Alere Afinion HbA1c, Alere Afinion AS100 Analyzer

B Predicate 510(k) Number(s):

K151809

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K192987</u>	<u>K151809</u>
Device Trade Name	Aina HbA1c Monitoring System 2	Alere Technologies AS Afinion HbA1c, Afinion AS100 Analyzer
General Device Characteristic Similarities		
Intended Use/Indications For Use	Intended to be used for the quantitative measurement of glycosylated hemoglobin (HbA1c) It is intended to monitor long term glycemic control of persons previously diagnosed with diabetes.	Same
Assay Method	Boronate affinity, photometry	Same
General Device Characteristic Differences		

Device & Predicate Device(s):	<u>K192987</u>	<u>K151809</u>
Sample Type	Anticoagulated venous whole blood in K2-EDTA	Capillary blood (from finger prick), Anticoagulated venous whole blood in EDTA, heparin, or citrate.
Measuring Range	4.4-13.4% HbA1c	4-15% HbA1c
Sample Volume	5 µL	1.5 µL
Test Time	3 minutes	3.5 minutes
Total Hemoglobin Range	7.2 – 20.0 g/dL	6-20 g/dL

VI Standards/Guidance Documents Referenced:

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline-Third Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures

CLSI EP07-A3: Interference Testing in Clinical Chemistry; Approved Guideline –Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Internal Precision

The sponsor conducted an internal precision study according to CLSI EP05-A3, using three (3) lots of the Aina HbA1c Test Kits and three (3) Aina HbA1c Monitoring System 2s. Three human venous whole blood samples (K2-EDTA) were collected with 5.4%, 6.1% and 11.1% HbA1c levels. Samples were measured in duplicate in two runs per day for 20 days producing n=80 results per sample per lot for a total of 240 results per sample. The within-run, between-run, between-day and total precision were calculated (SD and %CV). The results are summarized below:

Lot 1			Repeatability (Within-Run)		Between Run		Between Day		Total	
Sample	N	Mean HbA1c %	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Normal	80	5.3	0.2	3.5	0.06	1.2	0.2	3.0	0.2	4.0
Elevated	80	6.0	0.2	2.9	0.03	0.5	0.2	2.6	0.2	3.3
High	80	11.2	0.2	2.0	0.00	0.0	0.2	1.5	0.3	2.5

Lot 2			Repeatability (Within-Run)		Between Run		Between Day		Total	
Sample	N	Mean HbA1c %	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Normal	80	5.3	0.2	2.8	0.01	0.1	0.1	2.4	0.2	3.5
Elevated	80	6.1	0.2	3.1	0.01	0.2	0.1	2.3	0.2	3.6
High	80	11.3	0.3	2.8	0.09	0.8	0.3	2.4	0.3	2.7

Lot 3			Repeatability (Within-Run)		Between Run		Between Day		Total	
Sample	N	Mean HbA1c %	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Normal	80	5.5	0.2	3.0	0.1	1.8	0.1	2.2	0.2	3.1
Elevated	80	6.2	0.2	3.3	0.01	0.2	0.2	3.0	0.2	3.4
High	80	10.9	0.3	2.3	0.2	1.4	0.2	1.5	0.3	3.0

Total			Repeatability (Within-Run)		Between Run		Between Lot		Between Day		Total	
Sample	N	Mean HbA1c %	SD	CV%	SD	CV%	SD	CV%	SD	CV%	SD	CV%
Normal	240	5.4	0.2	3.6	0.06	1.2	0.1	2.4	0.1	1.7	0.2	4.2
Elevated	240	6.1	0.2	3.0	0.03	0.5	0.1	1.4	0.1	2.0	0.2	3.7
High	240	11.1	0.3	2.9	0.1	0.9	0.2	2.0	0.1	1.0	0.4	3.2

2. Linearity:

A linearity study was conducted in accordance with CLSI EP06-A. Testing was conducted using venous whole blood specimens collected in K2-EDTA tubes. Nine levels were prepared across the measuring range and tested in replicates of five on the Aina system in random order. Individual HbA1c readings for each intermediate dilution were plotted versus the expected HbA1c concentration. The linear regression equation is shown below:

$$y = 1.01x - 0.08 \quad R = 0.998$$

The linearity results support the sponsor's claims that the assay is linear across the reportable measuring interval of 4.4 to 13.4% HbA1c.

3. Analytical Specificity/Interference:

A study was performed as per CLSI EP07-A3 using the Aina HbA1c Monitoring System 2 to assess the known endogenous and exogenous substances that could interfere with the assay. The study was conducted using venous whole blood specimens collected in K2- EDTA with target HbA1c at the following levels following levels: <5.5% and Elevated 8-10 %. Each

blood sample was divided into two pools: a control sample and a test sample. The test sample was spiked with each interfering substance at two different concentrations and data was collected in fifteen replicates. If the lowest concentration of any interference sample tested failed to pass the acceptance criterion, it was diluted and re-tested. The sponsor defined non-significant interference as $\leq\pm 5\%$ deviation compared to the result of the control. Results demonstrated that no significant interference was observed for the following substances up to the listed concentrations.

Substance	Highest Level Tested with No Significant Interference
Acetylsalicylic Acid	65 mg/dL
Ascorbic acid	30 mg/dL
Acetaminophen	30 mg/dL
Bilirubin (conjugated)	35 mg/dL
Bilirubin (unconjugated)	66 mg/dL
Triglycerides	2000 mg/dL
Glyburide	20 mg/dL
Ibuprofen	50 mg/dL
Metformin	5.1 mg/dL
Cholesterol	500 mg/dL
Glucose	1500 mg/dL
Rheumatoid Factor	1000 IU/mL
Total Protein	9.3 g/dL
Fructosamine	750 μ mol/L
Rifampicin	6 mg/dL
Salicylic Acid	60 mg/dL

Cross-Reactivity: Hemoglobin Derivatives

A study was performed using the Aina HbA1c Monitoring System 2 to assess the effect of hemoglobin derivatives on the measurement of HbA1c. The study was conducted using venous whole blood specimens collected in K2- EDTA tubes with target HbA1c of <5.5% and 8-10%. Each blood sample was divided into two pools: a control sample and a test sample. Acetylated hemoglobin was derived in the presence of acetylsalicylic acid, carbamylated hemoglobin was derived in the presence of sodium cyanate, and labile A1c was derived in the presence of glucose. The test sample was spiked with each interfering substance at two different concentrations and data was collected in fifteen replicates. The sponsor defined non-significant interference as $\leq\pm 5\%$ deviation compared to the result of the control pool. The table below summarizes the results of this study.

Hemoglobin Derivative	Highest Level Tested with No Significant Interference
Acetylated hemoglobin	126.1 mg/dL (acetylsalicylic acid)
Carbamylated hemoglobin	32.5 mg/dL (sodium cyanate)
Labile hemoglobin	1000 mg/dL (glucose)

Hemoglobin Variants

A study was performed to evaluate the interference effect of hemoglobin variants, as found in patients with natural hemoglobinopathies, in the quantitative measurement of HbA1c using the Aina system on venous whole blood samples. This study was completed as per the CLSI EP07-A3 guidelines using venous whole blood patient samples containing at least one of the following variants: HbC, HbD, HbE, HbS, HbF or HbA2. For a particular Hb variant to be considered as not interfering with measurements on the Aina system, the relative percent difference estimated from the Deming regression analysis should be under $\pm 7\%$ at concentrations of approximately 6 %HbA1c and 9 %HbA1c. The studies demonstrate that The labeling contains the following information regarding hemoglobin variant interference:

WARNING: The Aina HbA1c assay has significant negative interference from Hemoglobin F (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin.

The results from the Aina HbA1c Monitoring System 2 show that there is no significant interference for samples containing Hemoglobin C ($\leq 50\%$), Hemoglobin D ($\leq 43\%$), Hemoglobin E ($\leq 31\%$), Hemoglobin S ($\leq 42\%$), and Hemoglobin A2 ($\leq 6.5\%$).

4. Assay Reportable Range:

4.4 - 13.4 % HbA1c.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

The Aina HbA1c Monitoring System 2 is traceable to the Diabetes Control and Complications Trial (DCCT) Method for Measurement of HbA1c. HbA1c values are reported according to the National Glycohemoglobin Standardization Program (NGSP) recommendations at the DCCT level. The system is certified with the National Glycohemoglobin Standardization Program (NGSP). See NGSP website for current certification at <http://www.ngsp.org>.

6. Detection Limit:

The claimed measuring range for the Aina HbA1c Monitoring System 2 is 4.4 to 13.4%.

7. Assay Cut-Off:

Not applicable.

8. Accuracy (Instrument):

See Section VII.B.1 Method Comparison Study.

9. Carry-Over:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

To demonstrate accuracy of the system, fresh prospective venous whole blood was collected with K2-EDTA as an anticoagulant from a total of 132 study participants at three (3) sites. The samples were tested in singlicate using three reagent lots and three devices (one each per site) by trained healthcare professionals in a laboratory environment. An additional sample from each participant was tested at an NGSP Certified Secondary Reference Laboratory (SRL) using the Tosoh G8 analyzer for comparator testing. The range of HbA1c tested was 4.4 to 13.4%. The results of the Aina HbA1c Monitoring System 2 were compared to the comparator method and linear regression analysis was performed using both Passing-Bablok and Weighted Deming analysis.

Regression analysis summary

Method	Slope	95% CI	y-Intercept	95% CI
Passing-Bablok	1.0	0.9792 - 1.041	-0.20	-0.4929 - 0.0377
Weighted Deming	1.003	0.9679 - 1.038	-0.1924	-0.4465 - 0.0618

2. Matrix Comparison:

Not applicable. The sponsor's only claimed anticoagulant is K2-EDTA.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

	NGSP	IFCC
Target in Diabetes	< 7.0%	< 53 mmol/mol

American Diabetes Association Standards of Medical Care in Diabetes 2018.

The labeling states:

Each laboratory should determine a reference interval that corresponds to the characteristics of the population being tested.

F Other Supportive Instrument Performance Characteristics Data:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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