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

A. 510(k) Number: K130014

B. Purpose for Submission:

New Device

C. Measurand:

Glycosylated hemoglobin (HbA1c)

D. Type of Test:

Quantitative, Immuno-turbidimetric assay

E. Applicant:

SAKAE Corporation

F. Proprietary and Established Names:

A1c Gear System

G. Regulatory Information:

1. Regulation section:

Classification Name	Product Code	Device Class	Regulation Number
Glycosylated hemoglobin assay	LCP	II	21 CFR 864.7470
Discrete photometric chemistry analyzer for clinical use.	JJE	I	21CFR 862.2160

2. Panel

81 Hematology

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

   The A1c GEAR System is intended for in vitro diagnostic use only for the quantitative measurement of the percent hemoglobin A1c (%HbA1c) from finger-stick blood or venous whole blood collected in in either EDTA or sodium fluoride (NaF) for clinical laboratory and point of care use. The measurement of HbA1c is recommended to monitor long-term glycemic control of persons previously diagnosed with diabetes mellitus. This test is not for screening or diagnosis of diabetes.

3. Special conditions for use statement(s):
   - For prescription use only.
   - This test is not for screening or diagnosis of diabetes.
   - Clinical settings and Point-of Care
   - This test should not be used in monitoring daily glucose control
   - Should not be used to replace daily home testing of urine and blood glucose levels
   - 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
   - Hemoglobinopathies may interfere with glycated hemoglobin analysis. Samples containing the following hemoglobin variants have been shown to interfere with this assay: Hemoglobin C, Hemoglobin D, Hemoglobin E, Hemoglobin F (>10%) and Hemoglobin S.

4. Special instrument requirements:

   A1c GEAR spectrophotometric analyzer

I. Device Description:

The A1c Gear System is comprised of a fully automated desktop electric spectrophotometer that measures HbA1c in human whole blood or finger-stick samples using a dedicated reagent (MEDIDAS HbA1c). The A1c Gear system shines light from a 660 nm LED (Light Emitting Diode) through the test material and measures the quantity of hemoglobin A1c in the total hemoglobin (HbA1c %) based on the lot-specific reagent parameters and changes in light absorbency caused by antigen-antibody reactions.

The MEDIDAS HbA1c Test Kit is comprised of a test cartridge, capillary, pipette tip and master calibration card. The cartridge is pre-filled with the reagent; latex (reagent R1), antibody and sample dilute solution (reagent 2).

The R1 Reagent contains:

- 0.3% w/v latex particles
- 0.2% w/v triethanolamine
- 0.02% w/v sodium hydrogen carbonate
- 0.02% w/v sodium azide

- 15 mM bicine buffer

The R2 Reagent contains:

- 0.002% w/v mouse monoclonal anti-human HbA1c antibody
- 0.0001% w/v goat anti-mouse IgG antibodies
- 1.3% w/v sodium chloride
- 0% w/v nonreactive ingredients
- 5mM bis-tris buffer

Controls are sold separately and are not part of the A1c Gear System.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Siemens DCA Vantage

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

   k071466
3. Comparison with predicate:

Similarities and Differences		
Item	New Device A1cGear and MEDIDAS HbA1c	Predicate Device Siemens DCA Vantage k071466
Intended Use	Quantitative measurement of the percent Hemoglobin A1c in human whole blood.	Same
Methodology	Immuno-turbidimetric	Same
Sample Type	Whole blood and finger stick samples	Same
Recommended Testing Environment	Professional and Point of Care Use	Same
Analytical Range	4.0-13.0%	2.5 – 14.0%
Reagent storage	2-8°C	Same

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

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices-5/11/2005

IEC 60601-1-2: 2007-Medical Electrical Equipment-Part 1-2: General requirements for Basic Safety and Essential Performance-Collateral Standard: Electromagnetic Compatibility Requirements and Tests.

IEC 60601-1:1995 – Medical Electrical Equipment Part 1: General Requirements for Safety. Version 1995

IEC 62304:2006- Medical Device Software-Software Life Cycle Processes. Version 2006

CLSI-EP06-A: Evaluation of the Linearity of Quantitative Measurement procedures: A Statistical Approach

CLSI-EP05-A2- Evaluation of Precision Performance of Quantitative Measurement Methods

ISO 14971:2007- Medical devices-Application of Risk Management to Medical Devices

L. Test Principle:

The A1c GEAR system is an immuno-turbidimetric method enhanced by latex particles using a two-reagent sequence. Hemolysate is mixed with the R1 reagent. Total Hemoglobin and HbA1c have the same absorption affinity for these particles, therefore the % of HbA1c present in the total hemoglobin is proportional to the latex-bound HbA1c. Addition of the R2 reagent leads to agglutination complexes, formed by the interaction between latex-bound HbA1c and the corresponding antibodies. Turbidity created by these aggregates is proportional to the amount of latex-bound HbA1c therefore is proportional to the % of HbA1c in the total hemoglobin.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Internal Precision Study

   Precision studies were performed according to CLSI EP5-A2 guideline. Within-run precision, between-run precision, between-day precision and total precision were determined using the A1c Gear System. The study included a Low whole blood control (5.2% HbA1c), a High whole blood control (9.0% HbA1c) and three EDTA whole blood samples collected from one non-diabetic patient and two diabetic patients (5.5%, 11.1% and 12.1% HbA1c respectively). Samples were analyzed in duplicate twice a day for 20 days. Results are shown below:

	N	Mean %HbA 1c	Within -Run		Between-run		Between-day		Total Precision	
			SD	CV%	SD	CV	SD	CV	SD	CV
Control L	80	5.2	0.07	1.26	0.00	0.00	0.03	0.51	0.07	1.36
Control H	80	9.0	0.08	0.85	0.05	0.58	0.02	0.26	0.10	1.06
Non-diabetic	80	5.5	0.04	0.73	0.02	0.29	0.04	0.80	0.06	1.12
Diabetic 1	80	11.1	0.12	1.11	0.04	0.39	0.08	0.70	0.15	1.37
Diabetic 2	80	12.1	0.14	1.14	0.00	0.00	0.12	1.01	0.18	1.52

External Precision Study

An external precision study was performed at 3 Point of Care sites using the A1c Gear System. Three whole blood control samples (~5.2, ~7.1,~ 11.0% HbA1c) and three EDTA whole blood samples (~5.8,~8.0 and ~11.0% HbA1c) were analyzed. The control samples were analyzed in duplicate for twice a day for 20 days and patient samples were analyzed in duplicate twice a day for a total of 10 days. Results are as shown below:

Sample	**N =**	**Site**	**Mean %HbA1c**	**Within-site CV (%)**	**Overall mean %HbA1c**	**Reproducibility Total CV (%)**
Control 1	120	1	5.19	2.85%	5.22	2.26%
	120	2	5.21	1.92%		
	120	3	5.27	1.46%		
Control 2	120	1	7.01	2.53%	7.06	2.11%
	120	2	7.07	1.73%		
	120	3	7.10	1.73%		
Control 3	120	1	11.05	3.37%	11.04	2.55%
	120	2	11.09	2.48%		
	120	3	11.00	1.35%		
Sample Low	60	1	5.80	3.14%	5.84	3.12%
	60	2	5.83	3.28%		
	60	3	5.89	2.63%		
Sample Middle	120	1	8.01	3.31%	8.07	4.16%
	128	2	7.87	2.30%		
	120	3	8.34	2.91%		
Sample High	120	1	10.55	3.22%	10.84	5.25%
	128	2	10.59	2.46%		
	120	3	11.38	3.21%		

b. Linearity/assay reportable range:

Linearity was evaluated according to CLSI-06A. The linearity of the A1c Gear System was verified using two EDTA whole blood samples, including a normal sample with HbA1c concentration of 4.0% and an elevated HbA1c level sample with HbA1c concentration at 15.0%. The normal and high samples were inter-mixed to make a total of 11 intermediate samples covering the assay range. All intermediate dilutions were analyzed in replicates of three with randomized run orders. The mean observed %HbA1c value was determined for each intermediate dilution and plotted versus the relative analyte concentration. The linear regression is as follows:

$y=0.98x+0.19$, $r^2=1.00$

The study supports the sponsors claimed linearity range of 4.0-13.1% HbA1c

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

Traceability: The A1c Gear System 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.

Value Assignment:

Sponsor recommends the use of the Bio-Rad Lyphochek Diabetes Control (k070546) as a commercially available external control to be used with this device.

Calibration:

Calibration is obtained by using a Master Calibration Card. The master calibration card is traceable to International Federation of Clinical Chemistry (IFCC) reference materials.

Stability:

The A1c GEAR System kit (Master calibration card and test cartridge) should be refrigerated at 2-8°C (36-46°F) and used immediately after opening. The expiration date of the Master calibration card and cartridge as stated on the package is 12 months after the date of manufacture.

d. Detection limit:

The Limit of Blank (LoB) was determined by assaying 90 replicates of a zero sample (blank) using the A1c Gear System.

Limit of Detection (LoD) was determined by assaying 27 replicates of three low HbA1c samples. Each sample was assayed using the A1c Gear System. Detection limits are summarized in the table below:

LoB	**LoD**
2.3%	2.6%

The assay has a reportable range of 4.0-13.1% HbA1c.

e. Analytical specificity:

An interference study was performed to assess common or known endogenous and exogenous substances that could interfere with the A1c Gear System. The potential interferents listed below were spiked into human EDTA whole blood samples with different levels of %HbA1c (~6.2% and ≥8.0% HbA1c). The %HbA1c values of the spiked samples were compared to reference samples (sample containing no interferent). Samples were tested in quadruplicate to give a total of four replicates per sample. The sponsor considered ≤ +/- 10% as their acceptance criterion. The interferent study results are summarized in the table below:

Potential Interferent	Highest concentration in which no significant interference was observed.
Unconjugated Bilirubin	37 mg/dL
Triglycerides	2,000 mg/dL
Conjugated Bilirubin	40 mg/dL
Rheumatoid Factor	550 IU/mL
Acetaminophen	20 mg/dL
Ibuprofen	50 mg/dL
Glibenclamide	0.2 mg/dL
Metformin	5.1 mg/dL
Ascorbic Acid	6.0 mg/dL

ii.) An interference study was performed to assess the effect of labile A1c, Carbamylated hemoglobin and acetylsalicylic acid with the A1c Gear System. Each interfering substances was tested using two EDTA whole blood samples with different levels of %HbA1c (~6% and > 9.0% HbA1c). Samples were spiked with the interfering substance and analyzed in duplicate. The percent difference of the samples with and without (reference sample) the potential interfering substance was calculated. The sponsor's acceptance criteria is analyte recovery should not vary from the base recovery by more than +/- 10%.

The sponsor concludes there was no significant interference with the following:

- Labile A1c concentrations up to 2000 mg/dL
- Carbamylated hemoglobin up to 10 mg/dL
- Acetylated hemoglobin up to 200 mg/dL

ii.)A hemoglobin variant study was performed using commercial samples known to contain Hemoglobin variants C, D, E, S and F. Samples contained both low and high levels of % HbA1c at concentrations from 4.2-11.6% HbA1c. These variant samples were tested in duplicate using the A1C Gear System. The results indicated samples containing Hemoglobin C were elevated by 24%, samples containing Hemoglobin D were elevated by 16%, samples containing Hemoglobin E were elevated by 13% and samples containing Hemoglobin S were elevated by 13%. Samples containing >10% Hemoglobin F were decreased by 22%. All variants tested were shown to interfere with this device.

The device labeling contains the following boxed warning:

"Hemoglobinopathies may interfere with glycated hemoglobin analysis. Samples containing the following hemoglobin variants have been shown to interfere with this assay: Hemoglobin C, Hemoglobin D, Hemoglobin E, Hemoglobin F (>10%) and Hemoglobin S."

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

An internal method comparison study was conducted using venous whole blood collected in K_2 EDTA. Samples ranged from 4.2-11.7 HbA1c% and were analyzed in singlicate. Samples were analyzed on the A1c Gear and compared to the Arkray HA-8170 analyzer, the Tosoh Bioscience G7 HPLC analyzer and the DCA Vantage analyzer. The linear regression is as follows:

Comparison Method	**N**	**HbA1c (%)**	**Regression Line**	**r^2**
Arkray-HA 8170 analyzer	158	4.6-10.6	y = 1.03x - 0.33	0.98
Tosoh G7 analyzer	40	4.2-9.8	y = 0.99x + 0.31	0.98
DCA Vantage analyzer	60	4.7-11.7	y = 0.95x - 0.12	0.99

An additional method comparison study was performed using finger-stick samples at 3 POC sites and analyzed on the A1c GEAR System versus venous EDTA whole blood samples collected from the same patients and analyzed on the Tosoh G8 analyzer. The samples tested spanned the range of 4.9-11.9% HbA1c to include the clinically relevant range. The results are as follows :

Study Site	N	Min	Max	Slope (95% CI)	Intercept (95% CI)	r
1	47	4.9	11.9	0.968 (0.941 to 0.994)	0.04 (-0.16 to 0.24)	0.995
2	41	5.4	10.8	0.976 (0.936 to 1.015)	0.12 (-0.15 to 0.40)	0.990
3	46	5.0	9.6	0.989 (0.952 to 1.027	0.08 (-0.18 to 0.35)	0.990

b. Matrix comparison:

A study was peformed using finger-stick whole blood, EDTA whole blood and NaF whole blood. A total of 78 donor samples were collected from site 1 using finger-stick and venous EDTA, 46 donor samples were collected from site 2 using finger-stick and venous NaF and 81 donor samples were collected from site 3 using venous EDTA and NaF. Samples tested ranged from 4.3-10.9% HbA1c. The linear regression analyses are as follows :

Matrices	n	HbA1c%	Regression	r^2
EDTA vs Finger-stick	78	4.3-9.0	y=0.96x-0.09	0.99
NaF vs. Finger-stick	46	4.8-8.8	y=1.04x-0.06	0.99
NaF vs. EDTA	81	5.3-10.9	y=1.01x+0.01	0.99

Venous whole blood collected in sodium fluoride and whole blood finger-stick samples have been shown to be acceptable for use with the A1c Gear System.

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):

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range[1]:

The American Diabetes Association (ADA) expected value range is 4.0-6.0% HbA1c for people without diabetes.

The American Diabetes Association's (ADA) most recent Clinical Practice Recommendation for diabetes specified a treatment goal of less than 7% and suggests additional action when HbA1c level is above 8%.

HbA1c Value	Glycemic Goal
<8% HbA1c	Less stringent
<7% HbA1c	General (Non-Pregnant Adults)
<6.5% HbA1c	More stringent

American Diabetes Association Standards of Medical Care in Diabetes 2012, 35 (Supplement1), S11-S63[1]

N. Instrument Name:

A1c Gear System

O. System Descriptions:

1. Modes of Operation:

   Fully automated desktop Spectrophotometric analyzer

   Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

   Yes_____ or No __X___

   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:

   Barcoding or Manual entry

4. Specimen Sampling and Handling:

   Sample is obtained via a capillary tube that is inserted into a sampling cartridge. A pipette tip is added to the sampling cartridge along with the capillary tube. The sampling cartridge which contains the capillary tube and the pipette tip are inserted into the sampling slot. Samples must be tested within one hour after inserting the capillary into the cartridge. The sampling door is closed and the system beeps to start the test. A barcode printed on the reagent cartridge is recognized by a barcode reader and verified to use the appropriate calibration values for the particular lot number of the test cartridge.

5. Calibration:

   The reagent kit contains a master calibration card. It is recommended to enroll the Master Calibration card after opening every reagent kit.

6. Quality Control:

   In the labeling the sponsor recommends that control measurements be assayed when installing the device, when using a new lot of reagent, when using a new shipment of reagent, when test results do not match other clinical findings or symptoms, when using the device or reagent that had been stored for long-term, when reagents are stored improperly, when training and confirming performance of new operators, following national and/or local regulations for the facility, at regular intervals determined by the laboratory procedures.

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

Not applicable

Q. Proposed Labeling:

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

R. Conclusion:

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