

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

A. 510(k) Number:

k093548

B. Purpose for Submission:

Modification to the sampling test cartridge and software changes

C. Measurand:

Glycosylated hemoglobin (HbA1c)

D. Type of Test:

Quantitative, immunoassay

E. Applicant:

MEC Dynamics Corporation

F. Proprietary and Established Names:

Avie™ A1C System

G. Regulatory Information:

Regulation section	Classification	Product Code	Panel
21 CFR §864.7470	II	LCP	81, Hematology

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The Avie™ A1C System test is a point of care system that quantitatively measures % A1C (glycated hemoglobin) in capillary and venous whole blood. The Avie™ A1C

System consists of the Avie™ A1C System Reader, Avie™ A1C System Test Cartridge and Avie™ A1C System Diluent. The test is for physician directed prescription home use and professional use to monitor glycemic control in patients with diabetes mellitus. Single use, auto-disabling lancing devices are to be used in the professional setting. The device cannot be used in patients with hemoglobinopathies of Hemoglobin C and Hemoglobin D.

3. Special conditions for use statement(s):

- Point-of-care and physician directed prescription home use
- Not for screening for or diagnosis of diabetes
- Should not be used to test patients with hemoglobinopathies of HbC or HbD

4. Special instrument requirements:

Avie A1C Reader

I. Device Description:

The Avie A1C Test System consists of the following:

Reader - has a molded plastic housing which contains the electronics, optics, motors for locating mechanisms, LCD display and the power button. A printer (optional) may be purchased for the reader.

Test cartridge – contains the following chemistries: antibody to A1c, antigen conjugate on a solid membrane support. It is packaged in groups of 15 cartridges/vial.

Diluent vial – containing 2% detergent buffered solutions with 0.6% sodium chloride.

Each vial of cartridges comes with its own vial of diluent. They are sold together as a set.

MEC Dynamics Corp. calibrates the Avie A1c Test System using National Glycohemoglobin Standardization Program (NGSP) certified laboratory value assigned blood samples. Lot specific information for test cartridges is transferred to the Avie A1c Reader by radio frequency identification (RFID).

J. Substantial Equivalence Information:

1. Predicate device name(s):

Avie A1c Test System

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

k091400

3. Comparison with predicate:

Similarities		
Item	Device	Predicate (k091400)
Indications for Use	Same	Used in the management and treatment of diabetes, for long-term glycemic control
Sample Type	Same	Venous and capillary Whole blood
Calibration	Same	Cartridge calibration is automatic via RFID
Methodology	Same	Quantitative immunoassay
Reagent Packaging	Same	15 cartridges in a desiccant lined, tamper evident container
Intended Users	Same	Professional and physician-directed home use
Throughput	Same	3 minutes per sample
Reagent Storage	Same	39-82° F (15-28° C)
Units of Measurement	Same	%A1c

Differences		
Item	Device	Predicate
Sample Preparation	Direct application, touch test cartridge to blood drop	Pipette 5 micL into diluent vial, invert 5 times
Diluent	15 mL dropper multi-use bottle	1.0 mL single use vial

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

EN ISO 14971 Medical Devices—Application of Risk Management to Medical Devices

EN ISO 13485 Medical Devices—Quality Management Systems; Requirements for Regulatory Purposes

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline, April 2003

FDA Guidance: Review Criteria for Assessment of Glycohemoglobin (Glycated or Glycosylated) Hemoglobin In Vitro Diagnostic Devices

L. Test Principle:

The Avie A1c Test System uses whole blood from either fingerstick or venous samples. The whole blood is directly applied to the sample port of a test cartridge. Insertion of the test cartridge into the reader automatically prompts the operator to add diluent. The diluent lyses

the red blood cells which allows both the A1c and total hemoglobin analytes to be measured at their own distinct wavelengths. Hemoglobin from the lysed cells is converted to methemoglobin and is read at 420 nm. The concentration of hemoglobin is directly proportional to the intensity of methemoglobin concentration. The A1c hemoglobin combines with any-hemoglobin antibodies conjugated to colored microparticles. After a predetermined time, the microparticle mixture is automatically released onto a reagent strip where the reacted and unreacted microparticles are separated and read optically. %A1c = (A1c/Total Hb) x 100.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

An internal precision study was conducted using 2 control samples analyzed twice/day for 20 days by two operators using 2 meters and one lot of test cartridges (n=80).

Results were as follows:

	Control 1			Control 2		
	Mean	SD	%CV	Mean	SD	%CV
Within Day	5.6	0.19	3.3	8.1	0.24	2.9
Between Day	5.6	0.17	3.0	8.1	0.19	2.4
Total	5.6	0.24	4.4	8.1	0.31	3.8

An external precision study was conducted at 3 point-of-care sites with 4 operators at 2 sites and 5 operators at one site. 3 meters and 2 cartridge lots were used across all sites. Each operator analyzed 3 whole blood samples with values ranging from <6% HbA1c, 6-7% HbA1c and 10-12% HbA1c, thrice per day.

Results are presented by site and total:

Site 1	Low Sample				Mid Sample				High Sample			
	n	Mean	SD	%CV	n	Mean	SD	%CV	n	Mean	SD	%CV
Between Day	4	5.81	0.09	1.49	4	8.55	0.23	2.68	4	11.45	0.22	1.90
Overall	15	5.81	0.11	1.89	15	8.55	0.23	2.72	15	11.45	0.30	2.64

Site 2	Low Sample				Mid Sample				High Sample			
	n	Mean	SD	%CV	n	Mean	SD	%CV	n	Mean	SD	%CV
Between	4	5.70	0.09	1.65	4	8.79	0.11	1.25	4	12.03	0.16	1.32

Day												
Overall	12	5.70	0.10	1.67	12	8.79	0.36	4.13	12	12.03	0.40	3.29

	Low Sample				Mid Sample				High Sample			
Site 3	n	Mean	SD	%CV	n	Mean	SD	%CV	n	Mean	SD	%CV
Between Day	4	5.67	0.12	2.20	4	8.47	0.06	0.72	4	11.22	0.16	1.40
Overall	12	5.67	0.16	2.85	12	8.47	0.20	2.38	12	11.22	0.22	2.01

	Low Sample				Mid Sample				High Sample			
Combined Site	n	Mean	SD	%CV	n	Mean	SD	%CV	n	Mean	SD	%CV
Between Day	13	5.73	0.11	1.96	13	8.60	0.20	2.34	13	11.56	0.38	3.32
Between Sites	3	5.72	0.07	1.28	3	8.60	0.17	1.96	3	11.57	0.42	3.63
Overall	39	5.73	0.14	2.37	39	8.60	0.30	3.45	39	11.56	0.45	3.93

b. Linearity/assay reportable range:

Two natural whole blood samples with values of 13-14% HbA1C and 4.5-5.5% HbA1C were mixed in varying proportions to make 11 test samples spanning the measuring range of the device. Testing was performed in quintuplicate on one Avie A1c Test System with one lot of test cartridges. HbA1c recoveries of the observed versus the expected concentrations were 98-104% across the measuring range. Linear regression is:

$$y=0.9757x + 0.2261, r^2 = 0.9963$$

Based on the data in this study, the measuring range of the Avie A1c is 5-14% HbA1c.

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

Controls:

External control materials are purchased separately (k060570). See item O.6 below for labeling recommendations.

Cartridge Stability:

Open and closed vial cartridge stability was tested at specified time intervals in real time at 2-8° C, 21-25° C and 36-38° C. Studies support the labeling for six month open cartridge vial stability at 21-25°C and closed vial cartridge stability for one year at 21-25°C. Humidity studies were performed from 10-80% RH and support storage of open and closed vials between 10-80% relative humidity. Shipping studies were performed where cartridges were stored at 37° C for three days and then stored at 2-8° C and 25° C for up to six months. Variable storage conditions were also tested where cartridges were moved from room temperature storage to 2-8° C and back again. Performance supported the expiration dating in the labeling.

Diluent Stability:

Closed vial and open diluent stability was tested at specified time intervals in real time at 2-8° C, 18-25° C, 36-38° C and 44-46° C with three diluent lots. Studies support the labeling for closed vial stability for 12 months at 18-25° C and open vial stability for 6 months at 18-25° C. Humidity were performed from 10-80% RH. Studies support storage of open and closed vials between 10-80% relative humidity. Studies support six months stability for open vials at 18-25° C. Shipping studies were performed where cartridges were stored at 45° C for three days and then stored at 25° C for up to 12 months. Variable storage conditions were also tested where cartridges were moved from room temperature storage to 2-8° C and back again. Both the shipping and variable storage condition performance supported the expiration dating in the labeling.

Traceability:

The sponsor has documented traceability to the NGSP's recommended accuracy base for HbA1c by performing a direct comparison with a Secondary Reference Laboratory (SRL) using 40 fresh human specimens. The assay is NGSP certified for 2011. However, NGSP certification expires at the end of one year. For current certifications, see the NGSP website at: <http://www.ngsp.org/docs/methods.pdf>

d. Detection limit:

See item M.1.b., Linearity, above.

e. Analytical specificity:

Studies were performed to assess common or known substances that could interfere with the assay using multiple meters (3) and lots of diluent (2). Potential interferents were tested at their highest therapeutic levels. Whole blood samples with A1c% concentrations of 5-7% and 9-12% were evaluated in quintuplicate for each interferent. All samples had total hemoglobins within the reference range. Observed A1c% values were compared to the control samples whose A1c% was determined by

a NGSP certified method. The sponsor states that recovery within 10% of the control results was considered to be non-interfering. Results are summarized below:

Interferent	Test Conc. (mg/dL)	Sample 1, % A1c neat 5-7%	% Recovery	Sample 2, % A1c neat 9-12%	% Recovery
Acetaminophen	3.0	5.5	98 %	10.3	98 %
Acetylsalicylic acid	39.1	6.5	99 %	11.0	102 %
Ascorbic acid	2.0	6.3	104 %	10.2	97 %
Glibenclamide	1.28	5.7	91 %	10.6	95 %
Ibuprofen	7.0	6.7	102 %	10.6	98 %
Metformin	0.66	6.8	107 %	9.4	92 %
Triglyceride	3,280	6.0	97 %	10.0	90%
Bilirubin	20.0	6.8	102 %	11.7	98%
Labile glycated Hb	9.9	6.5	98 %	12.9	96%

The effect of total hemoglobin concentrations on the ability of the Avie A1c Test System to measure hemoglobin A1c was evaluated by using 3 whole blood pools with A1c concentrations of approximately 5-6%, 6.5-7%, and 9-11%. The pools were divided into 4 aliquots. The total hemoglobin for each aliquot was adjusted to approximately 5.0, 10, 15 and 21 g/dL total hemoglobin. Total hemoglobin concentrations were confirmed on a commercially available hematology device and the A1c concentrations were confirmed on a NGSP certified device. HbA1c recovery on the Avie Test System needed to be within $\pm 10\%$ of the target value for each total hemoglobin concentration. Each sample was analyzed 5 times on one meter and one lot of cartridges. Recoveries ranged from 98-104%. No significant (no more than $\pm 10\%$) effect from total hemoglobin between 5 and 21 g/dL was observed.

To evaluate the effect of labile glycated hemoglobin, two whole blood samples representing normal and diabetic A1C concentrations were incubated at 37° C for 4 hours in the presence of 1,100 mM glucose. Recoveries were compared to non-incubated aliquots of the non-incubated whole blood samples. Interference is defined as recovery >10% of the non-incubated samples. No significant effect from labile A1c was observed (see results above).

Hemoglobin variants Hb S, C, F, D and E were evaluated on 15 fresh whole blood samples with total hemoglobin concentrations of 8.1-21.6% and HbA1c levels of 5.1-14.5%. Recoveries were compared to the NGSP reference laboratory. Interference was defined as recovery >10%. Samples containing HbF showed no significant interference up to 20.5% HbF. No significant interference was observed for HbS or E. Hemoglobins C and D had recoveries > 10%.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

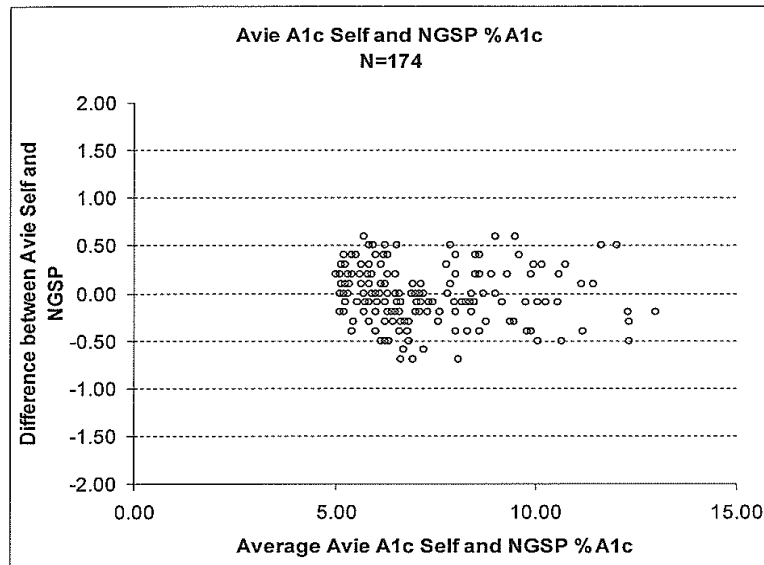
A lay-user study was performed at four Point-of-Care sites with a total of 174 lay-users and four POC health care professionals using 6 test cartridge lots and 12 Avie A1c readers. The lay-users ranged in age, education and were equally divided between males and females. Type-I diabetics, type-2 diabetics or non-diabetics participated in the study. Each participant performed a finger stick and tested their blood using only the labeling instructions. A trained professional then performed another finger stick, and a venipuncture to test both samples. Lay user fingerstick results from the Avie A1C were compared to another NGSP certified fingerstick system and to the venous blood, which was analyzed in a NGSP laboratory (Columbus, MO). %A1c concentrations ranged from 5.0% to 14.0%.

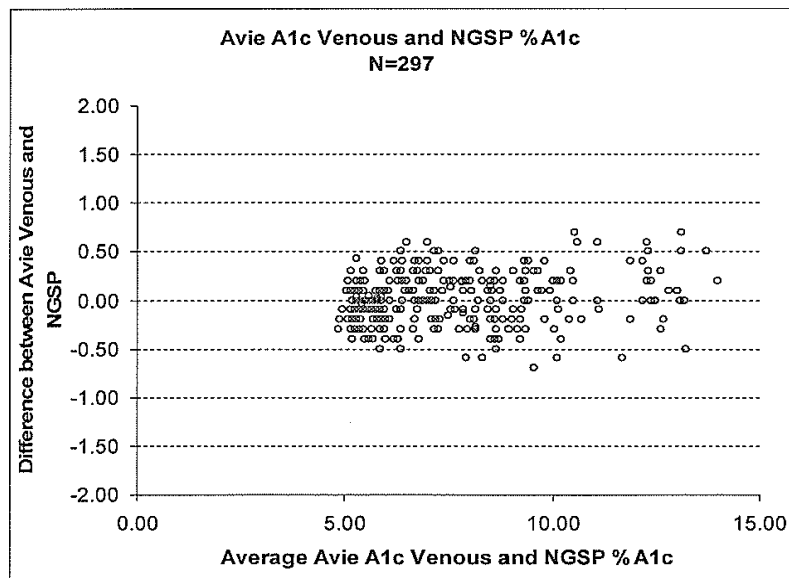
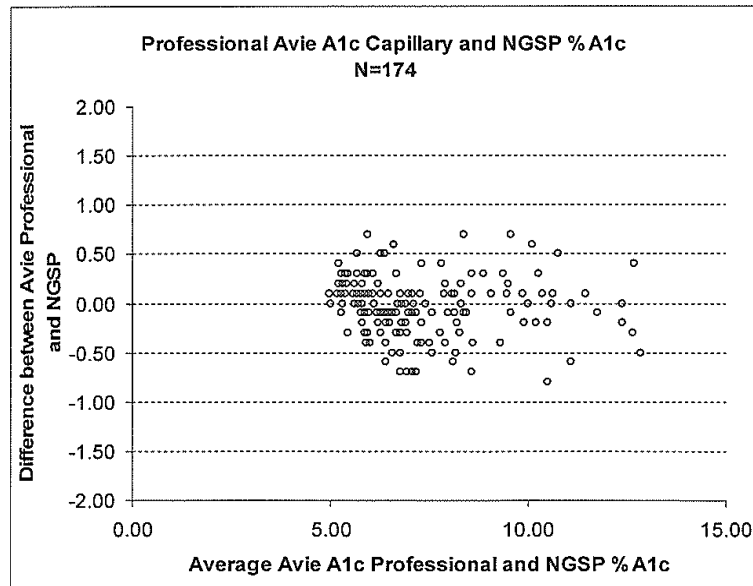
An additional 126 banked and fresh venous samples were obtained and distributed among two sites. These samples were analyzed by healthcare professionals at each site. All venous sample results were compared to a NGSP laboratory (Columbus, MO). The results are presented below:

	n	Slope (95% CI)	Intercept (95% CI)	r
Lay user fingerstick vs. NGSP	174	0.976 (0.952, 0.999)	0.151 (-0.025, 0.326)	0.987
Professional fingerstick vs NGSP	174	0.973 (0.951, 0.997)	0.172 (0.000, 0.343)	0.988
Professional venous vs NGSP	297	0.972 (0.959, 0.986)	0.210 (0.104, 0.316)	0.993

Bland Altman Plots for each study is below:

Bland Altman Plots:





b. *Matrix comparison:*

See Method Comparison above.

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:

In the labeling the sponsor presents the American Diabetes Association target for well controlled diabetes which is less than or equal to 6.5% HbA1c.¹

¹Diabetes Care, Volume 33, Supplement 1, January 2010

N. Instrument Name:

Avie A1c Reader

O. System Descriptions:

1. Modes of Operation:

The reagent test cartridges are single use and must be replaced in order to perform a new test. The diluent vial is for use with multiple cartridges.

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 sample identification function with this device. Samples are applied directly to the test cartridge as they are collected.

4. Specimen Sampling and Handling:

Fingerstick capillary whole blood, or a drop of venous whole blood is directly applied from the finger or vial to the cartridge test port. The cartridge is inserted into the reader and diluent is added to the test port at the prompt.

5. Calibration:

The Avie A1c reader is factory calibrated and is not field or user adjustable. Strip lot numbers are scanned into the Avie A1c reader via RFID.

6. Quality Control:

The Avie A1c Reader has an internal control system that performs operational self-checks (optics and software) when the device is turned on. If a malfunction is detected the reader will display an error message. The sponsor recommends that 2 levels of external controls be tested prior to running the first patient of the day, at least monthly if the device has not been used, every 3 months to check storage conditions, to become familiar with the testing process, to perform training or retraining of testing personnel, and whenever Avie A1c results do not match other clinical findings or symptoms. The sponsor recommends that the user contact them for recommendations on the external QC materials to use.

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

1. Studies were performed to examine the effects of variable whole blood sample size on the accuracy of the Avie A1c Test System. One lot of test cartridges and one lot of diluent were used on one meter. Samples ranging from 10-20 g/dL of total hemoglobin were tested using blood volumes between 0.5-6.0 micL. Samples were analyzed in quintuplicate. Results needed to be within $\pm 10\%$ of the A1c concentration as determined by an NGSP certified method. Data demonstrated that 5-6 micL of blood were acceptable. Labeling recommends the cartridges are wiped of excess blood prior to testing. The cartridges are designed to hold 6 micL of blood.
2. Studies were performed to examine the effects of variable diluent amounts on the accuracy of the Avie A1c Test System. Two lots of cartridges, two lots of diluent and one meter were used. Samples ranging from 10-20 g/dL of total hemoglobin were tested with 1-4 drops of diluent at one HbA1c concentration. Samples were analyzed in quintuplicate for each amount of diluent. Results needed to be within $\pm 10\%$ of the A1c concentration as determined by an NGSP certified method. Data demonstrated that 2, 3 or 4 drops of diluent were acceptable. One drop of diluent gave an error message on the device. Labeling recommends 2 drops of diluent.
3. Studies were performed to examine the effects of variable timing between collecting the blood on the test cartridge and adding the diluent. Labeling recommends collecting the blood on the test cartridge and immediately inserting the cartridge into the meter. The meter display prompts the user to “Add Diluent”. The protocol was performed using one cartridge lot, one diluent lot and one meter. Samples ranging from 10-20 g/dL of total hemoglobin at one HbA1c concentration were used in the study. Samples were analyzed in quintuplicate for each time interval. Blood was collected onto the test cartridge according to the labeling instructions and allowed to

4. The device is intended for point-of-care or physician directed home use. Disinfection studies were performed on the Avie A1C meter by an outside commercial testing service to determine the robustness of the meter to the recommended cleaning and disinfection protocol, and its effectiveness in preventing the spread of bloodborne pathogens, particularly hepatitis B virus (HBV). Fresh 10% bleach solution (EPA Reg. No: 5813-50) were validated, demonstrating complete inactivation of live virus for use with the meter. The sponsor also demonstrated that there was no change in performance or in the external materials of the meter after 650 disinfection and 650 cleaning cycles designed to simulate 3 years of healthcare professional and home use.
5. Demographic and usability questionnaires were completed by the 188 lay users. Based on the information provided, the sponsor concluded that the lay users were representative of the US population and 89% found the device very usable, 1% found the device difficult/somewhat difficult and 10% did not respond to the survey
6. The Avie A1c reader demonstrated the appropriate error codes in the following software verification and validation activities:
 - operation was outside of the recommended temperatures of 18-30° C,
 - inserting a used cartridge into the device.
 - sample total hemoglobin concentrations were above 20 g/dL or below 9 g/dL
 - A1c% >14%, A1c% < 5%A1c% results were synchronized between the reader display and the printer

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.