

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

A. 510(k) Number:

k081269

B. Purpose for Submission:

New device

C. Measurand:

Glycosylated Hemoglobin (HbA1c)

D. Type of Test:

Quantitative, immunoassay

E. Applicant:

MEC Dynamics Corporation

F. Proprietary and Established Names:

Avie™ A1C Test System

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LCP- Glycosylated hemoglobin assay	Class II	21 CFR 864.7470	81, Hematology

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The Avie A1C test is a point of care system that quantitatively measures % A1c (glycated hemoglobin) in capillary or venous whole blood samples. The test is for prescription use and physician directed home use to monitor glycemic control in patients with diabetes. The device can not be used in patients with the following hemoglobinopathies: HbF, HbC and HbD.

3. Special conditions for use statement(s):

Point-of-care and physician directed prescription home use

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.

Test cartridge – contains the following chemistries: antibody to A1c, antigen conjugate on a solid membrane support.

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

Pipette, pipette tips quick reference guide and user manual

J. Substantial Equivalence Information:

1. Predicate device name(s):

G5 I/II HbA1c Test System, Provalis Diagnostics Ltd. And Bayer A1cNow+

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

k041635 and k071466 respectively

3. Comparison with predicate:

Similarities/Differences			
Item	Device	G5 I/II	<u>Bayer A1c Now+</u>
Intended Use	Quantitative measurement of the percent of glycated hemoglobin	Same	<u>Same</u>
Indication for Use	Used in the management and treatment of diabetes, for monitoring long-term glycemic control	Same	<u>Same</u>
Sample	Whole blood	Whole blood	<u>Whole blood</u>
Methodology	Immunoassay and general chemistry	Rapid Affinity Chromatography	<u>Immunoassay</u>
Calibration	Cartridge has built-in reference calibration	Factory calibrated	<u>Factory calibrated</u>
Throughput	5 minutes/sample	7 minutes/sample	<u>5 minutes/sample</u>
Reagent storage	18-28°C	2-8° C	<u>Room temperature</u>

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

None were referenced

L. Test Principle:

The Avie A1c test system utilizes immunochemistry and general chemistry to quantify %A1c (glycated hemoglobin) in whole blood. The test consists of two distinct quantitative areas of measurement. The first area is a chamber where the met-hemoglobin is photometrical read at 420 nm. The optical density of the met-hemoglobin is proportional to the concentration of total hemoglobin. The second area is a mixing chamber where the diluted blood is mixed with anti hemoglobin antibodies conjugated to blue microparticles. After a predetermined time the microparticle mixture is automatically released onto a reagent strip where the reacted and un-reacted microparticle species are separated and read optically. The concentration of those species is used to calculate the amount of A1c.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision studies were conducted in-house by testing aliquots from a frozen blood sample with normal HbA1c and another frozen sample with elevated HbA1c. The samples were assayed twice a day for twenty days by multiple operators. The results are presented in the table below:

	Normal sample			Abnormal Sample		
	Mean	SD	%CV	Mean	SD	%CV
Within Day	6.1	0.22	3.6	8.9	0.32	3.5
Between day	6.1	0.16	2.6	8.9	0.34	2.7
Overall	6.1	0.30	5.0	8.9	0.40	4.4

External Precision

An external reproducibility study was performed in four Point-of-Care sites with four operators (one at each site). One level of control material was used in all four sites and assayed once each day of testing. The data is presented below:

	Level 1			
	n =	mean	SD	% CV
Site 1	6	5.7	0.4	7.3
Site 2	9	6.0	0.3	4.8
Site 3	8	5.0	0.3	5.9
Site 4	5	5.1	0.4	7.1

An additional external reproducibility study was performed at three sites with six operators (two at each site) for 5 days. Two levels of control material were tested at each site. The data is presented below:

		Control Level 1		Control Level 2	
		Between Day	Overall	Between Day	Overall
Site 1	Mean	5.52	5.52	8.76	8.86
	SD	0.18	0.28	0.54	0.45
	%CV	3.2	5.0	6.2	5.0
Site 2	Mean	6.13	6.13	8.5	8.50
	SD	0.08	0.12	0.41	0.47
	%CV	1.3	1.9	4.8	5.5
Site 3	Mean	5.91	5.91	8.38	8.38
	SD	0.21	0.36	0.49	0.64
	%CV	3.6	6.1	5.8	7.6

b. *Linearity/assay reportable range:*

The linearity range for the assay was assessed by inter-mixing a low blood sample with a high blood sample to make two sets of samples, one containing 8 and the other containing 7. The samples were assayed and the percent recoveries were calculated. The measuring range of the assay is 5-14%. The results are presented below:

Sample	Expected % A1C	Observed % A1C	Recovery
1	4.9	5.2	107%
2	6.2	6.6	107%
3	7.1	7.2	101%
4	8.0	8.7	109%
5	8.9	8.4	94%
6	9.8	8.9	91%
7	10.7	10.6	99%
8	11.6	11.4	98%
$y = 0.8626 + 1.118 R^2 = 0.956$			

Sample	Expected % A1C	Observed % A1C	Recovery
1	7.8	7.1	91%
2	8.8	8.3	94%
3	9.7	9.3	95%
4	10.7	9.8	92%
5	11.6	11.3	97%
6	12.6	12	95%
7	14	13.4	96%
$y = 1.009 + 0.6865 R^2 = 0.993$			

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

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. At this time, the assay is NGSP certified. However, NGSP certification expires at the end of one year. For current certifications see the NGSP website at: <http://www.ngsp.org/prog/index2.html>

d. *Detection limit:*

The reportable range is 5 to 14% HbA1c (see linearity section above).

e. *Analytical specificity:*

Studies were performed to assess common or known substances that could interfere with the assay. Potential interferents were tested at their published highest therapeutic

levels using two whole blood (one with normal and an abnormal A1c, both have normal hemoglobin level) samples. The sponsor states that recovery within 10% of the control results was considered to be non-interfering Results are presented in the table below:

Interferent	Test Concn. mg/dL	Sample 1 % A1c Neat 5%	% Recovery	Sample 2 % A1c Neat 9-12%	% Recovery
Acetaminophen	3.02	5.0	94	9.3	93
Ascorbic Acid	2.01	5.0	94	10	94
Metformin	0.39	5.1	95	11.2	112
Acetylsalicylic Acid	39.06	5.3	109	10.2	104
Glybenclamide	0.02	5.1	106	8.7	79
Ibuprofen	7.00	5.1	102	10.9	99
Triglyceride	3260	5.9	91	9.5	91
Bilirubin	20	4.4	102	11.9	100

The data demonstrates that the Avie A1c test system is sensitive to high levels of Glybenclamide and Metformin. These interferents are noted in the labeling.

To evaluate effect of hemoglobin concentrations, two whole blood (with normal A1c and abnormal A1c) samples were prepared to obtain five different hemoglobin concentration. The sponsor states that recovery within 10% of medium total Hemoglobin (12 mg/dL) was considered to be non-interfering. The results are presented in the table below:

Sample	Total Hb equivalent g/dL	% A1c	% Recovery
Sample 1	8.2	5.3	99
	9.3	4.8	91
	10.3	5.0	93
	12.3	5.3	100
	17.7	7.7	92
Sample 2	8.2	8.6	117
	9.3	7.0	94
	10.4	7.8	105
	12.2	7.4	100
	19.8	12.6	99

Testing demonstrated that the assay will perform over a hemoglobin range of 9-20 g/dL.

To evaluate the effect of labile glycated hemoglobin, two whole blood samples

representing normal and diabetic A1C were incubated at 37° C for 3-4 hours in the presence of 1400 mg/dL glucose. Sponsor states that recovery within 10% of control sample was considered to be non-interfering. The sponsor concluded that labile A1C concentrations across the assay range do not interfere with the assay.

To evaluate the effect of hemoglobin variants such as Hgb S, C, F, D and E, twelve samples collected from patients with known hemoglobin genetic variants were tested. Sponsor states that a substance was considered to show no significant interference if the difference between test sample and the blank sample was <10%. Samples containing HbS and HbE showed no interference. Samples containing HbC, F and D showed significant interference; this information is in the limitations section of the labeling.

f. Assay cut-off:

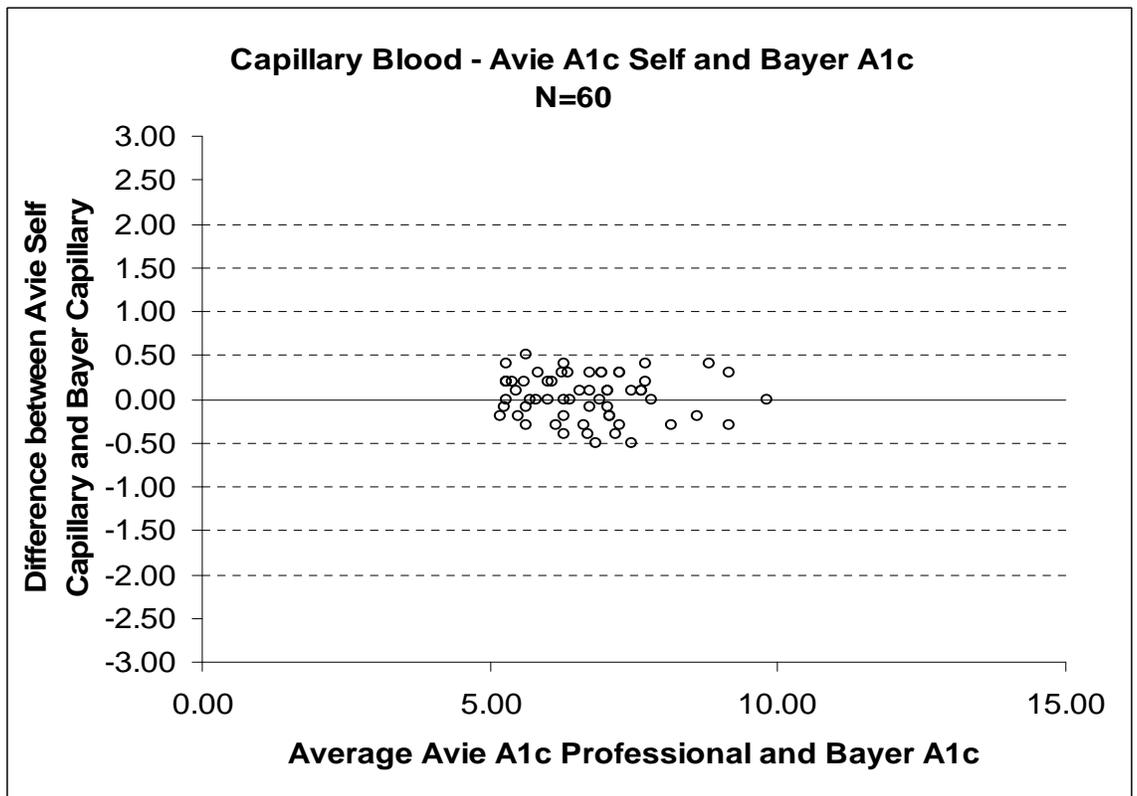
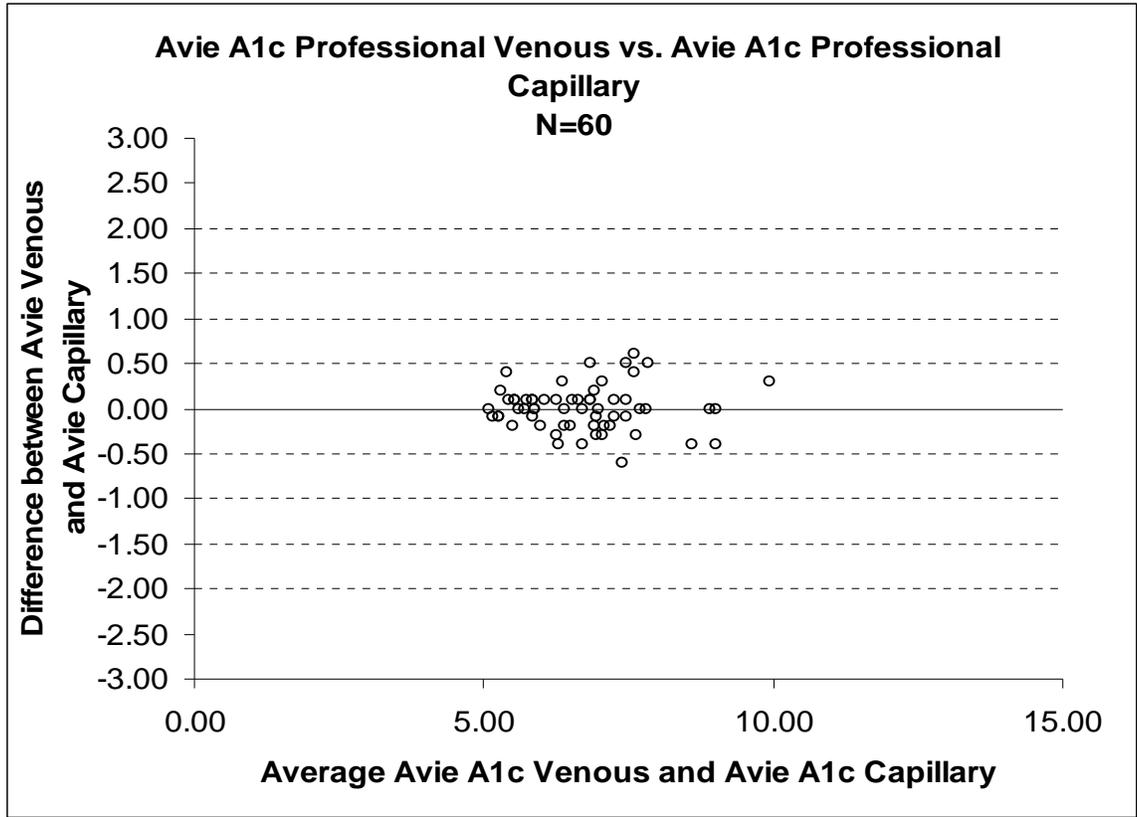
Not applicable

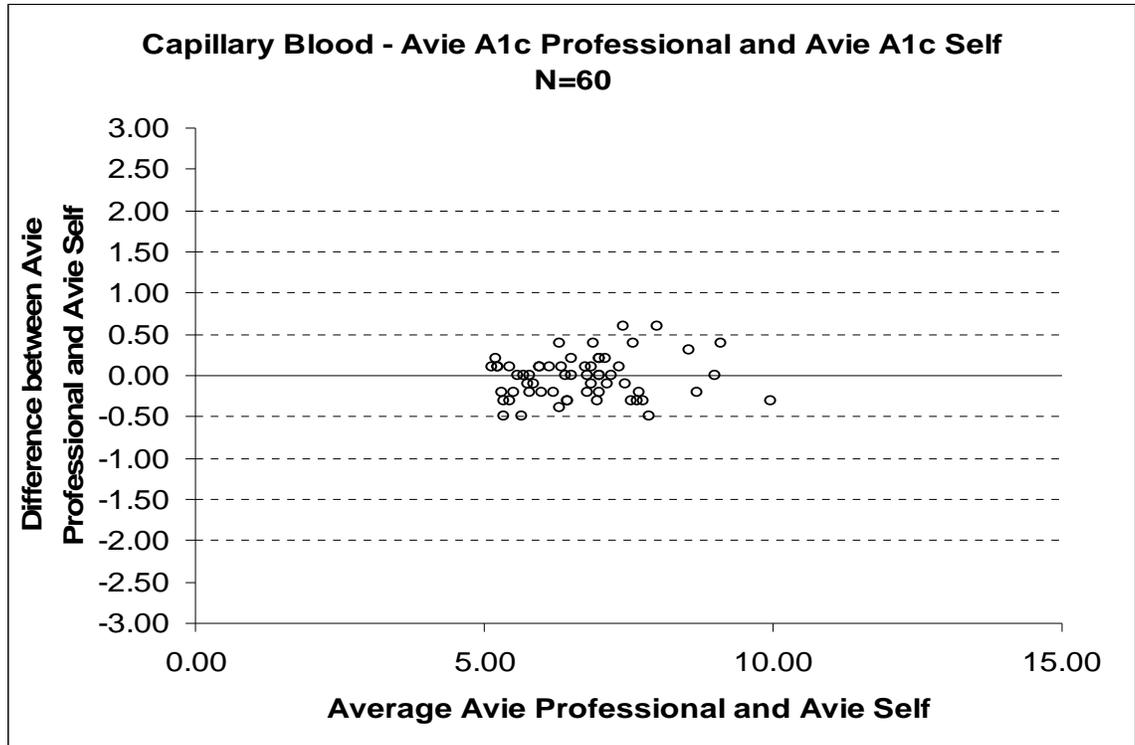
2. Comparison studies:

a. Method comparison with predicate device:

The lay-user study was performed at Point-of-Care site with a total of 60 lay-users and three point of care testers. The lay-users ranged in age, education and were equally divided between males and females; and were type-1 diabetics, type-2 diabetics or non-diabetics. Also, samples previously collected were used to help span the range of the assay. Each participant performed a finger stick and tested their blood using the instructions. A trained professional then performed another finger stick, testing the blood on the same lot of test cartridges. Venous samples were then drawn and compared to the results obtained on the Bayer A1c Now Plus. A questionnaire from the lay-users indicated that the device was easy to use. The results are presented below:

	Number of samples	Linear Regression	r value	Sample Range (mg/dL)
Professional finger stick vs Bayer	60	$y = 0.972x + 0.191$	0.947	5.2-10%
Lay-user finger stick vs Bayer	60	$y = 0.993x + 0.20$	0.946	5.2-10%
Professional finger stick vs Lay-user fingerstick	60	$y = 1.004x - 0.058$	0.946	5.2-10%





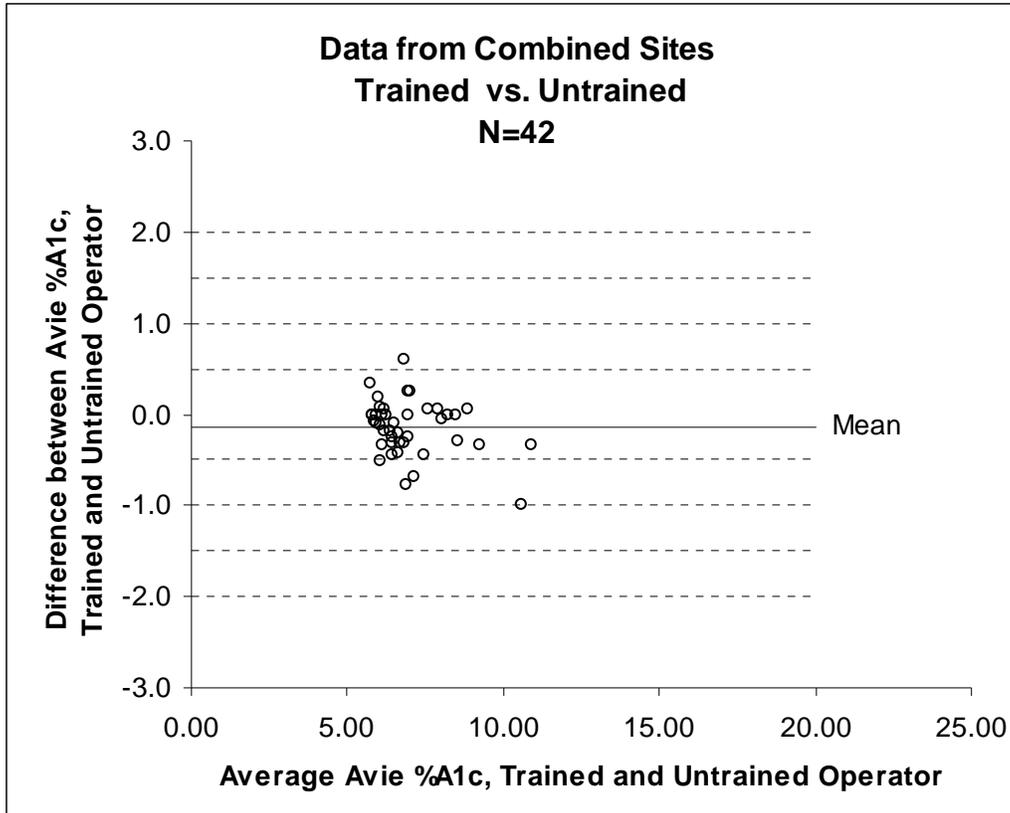
An additional method comparison study was performed to show that intended users at these sites could perform the test using only the labeling. The testing was performed at 3 sites with 6 untrained operators over 5 days. There were a total of 42 samples ranging from 5.8-10.7%. The linear regressions are as follows:

Site 1 - $y = 1.05x - 0.0175, r^2 = 0.94$

Site 2 - $y = 1.02x - 0.049, r^2 = 0.98$

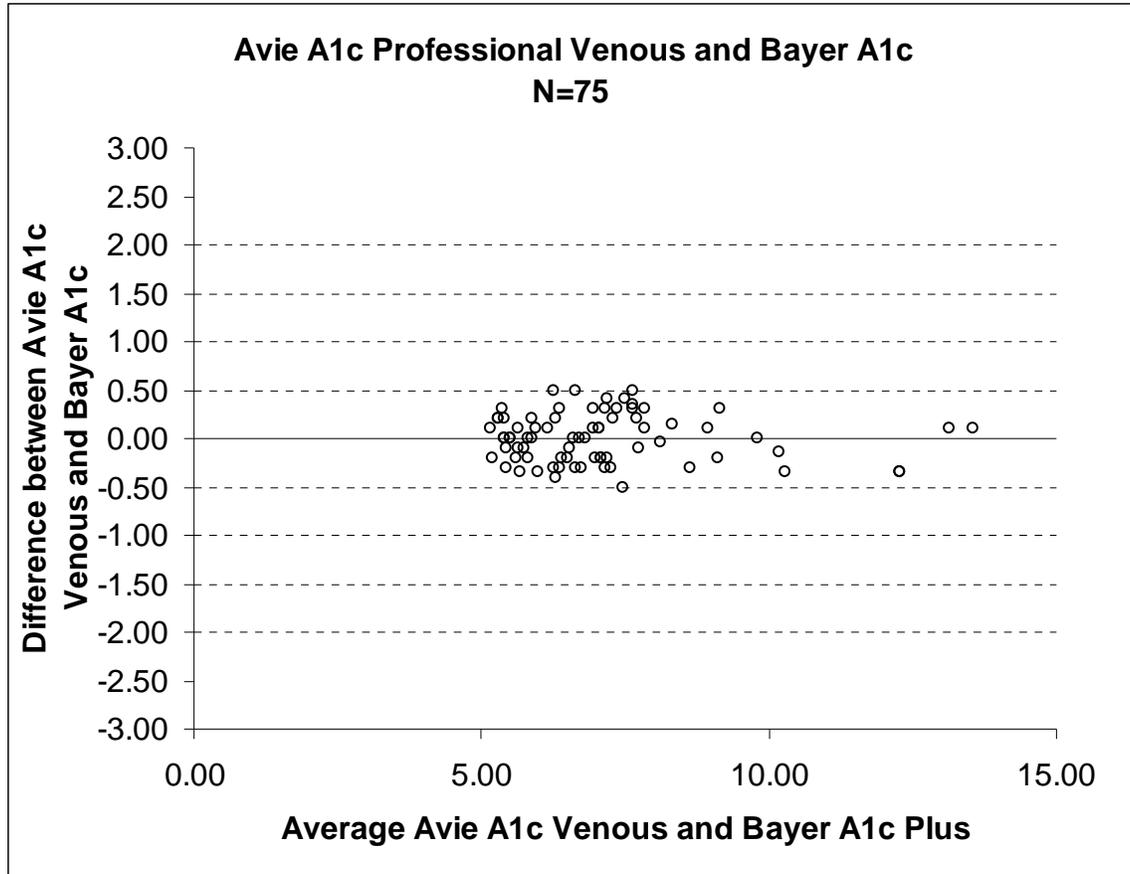
Site 3 - $y = 1.03x - 0.1335, r^2 = 0.93$

Combined - $y = 1.05x + 0.1899, r^2 = 0.95$



b. Matrix comparison:

75 EDTA venous whole blood samples were assayed on the Avie A1c and compared to the Bayer A1c Now Plus. Sample ranged from 5.2-13.5%. The linear regression is $y = 1.000x + 0.004$, $R^2 = 0.981$.



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:

American Diabetes Association target for well controlled diabetes is less than or equal to 7% A1C.

N. Instrument Name:

Avie A1c Reader

O. System Descriptions:

1. Modes of Operation:

Each diluent solution vial and reagent test cartridge are single use and must be replaced in order to perform a new test.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes or No

3. Specimen Identification:

There is no sample identification function with this device. Samples are applied directly to the test strip as they are collected.

4. Specimen Sampling and Handling:

The sample is collected using the blood collection device, which is a pipette manufactured to draw the exact sample volume from a finger-stick. The sample is then dispensed into the diluent vial. The vial is inverted 5 times to mix the blood with the diluent. Three drops of the mixture are added to the application well of the cartridge (which has already been inserted into the instrument).

5. Calibration:

The Avie A1c reader is factory calibrated and is not field or user adjustable.

6. Quality Control:

The Avie A1c Reader has an internal control system that performs operational self-checks (optics and software) when the reader is turned on. If a malfunction is detected the reader will display an error message. MEC Dynamics recommends that external controls be tested prior to home testing or at the start of each testing day, upon receipt of each new shipment or use of a new lot of cartridges, whenever storage room conditions have been above 28°C, to become familiar with the process or 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:

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.