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Multi-Center Accuracy Assessment of A1CNow®+: A Disposable System for Monitoring Hemoglobin A1c

Keith A. Moskowitz[1], Karmen Mercer[1], Emily Suscha[1], Maria Shafai[1], Corina Lindke[1], Charles Xie[1], James H. Anderson[1], Carrie Jo Szablowski[1], Beatriz Walsh[2], Stephanie Mihane[3]

BACKGROUND

Hemoglobin A1c (HbA1c) is indicated for diagnosis of diabetes using clinical laboratory (CL) analyzers. Point-of-Care (POC) HbA1c analyzers provide an advantage in fast turn-around-time which leads to immediate feedback of results, provider/patient discussion, and better disease management. POC HbA1c analyzers are not indicated for diabetes screening due to perceived inaccuracy. College of American Pathologists (CAP) criteria allow ±6% bias and the World Health Organization (WHO) allows POC when it is the only option or when a quality assurance (QA) program exists. The PTS Diagnostics A1CNow+ system is FDA cleared and CLIA waived, thus not subject to mandatory laboratory QA and proficiency testing. The A1CNow+ system is intended to monitor glycemic control for people with diabetes. Accordingly, the accuracy of PTS Diagnostics A1CNow+ system was evaluated relative to three clinical laboratory HbA1c analyzers.

The A1CNow+ system combines microelectronics, optics, and dry-reagent chemistry strips within a reusable, self-contained, integrated handheld monitor and single-use test cartridge. The A1CNow+ system is calibrated to an NGSP-certified reference analyzer and perform over 50 internal quality control checks when performing a test.

METHODS

The study was conducted at three U.S. wellness centers with three clinical laboratory analyzers:

- Roche Cobas® 6000
- Roche Cobas Integra 800
- Abbott Architect

For reference, the comparative measurements were performed on the Tosoh G8 analyzer.

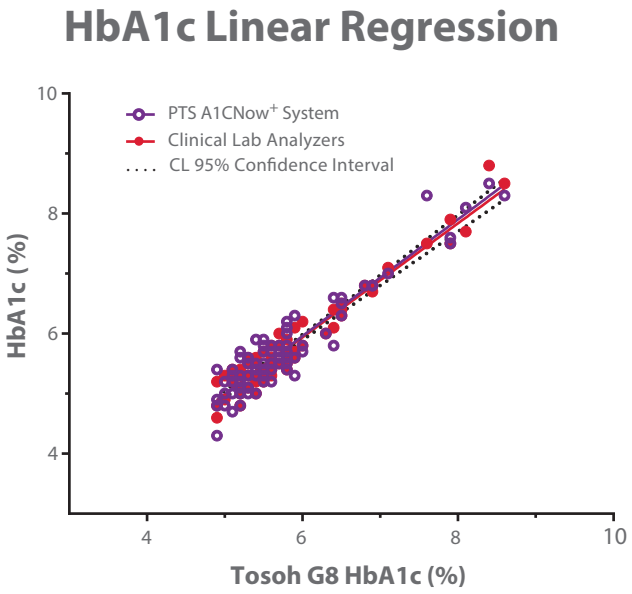
For this study, blood from 94 subjects was obtained and analyzed on the A1CNow+ system (fingerstick), clinical laboratory analyzers (EDTA venous blood), and the Tosoh (heparin venous blood). Correlation regression analysis was performed to determine accuracy and percent difference to assess bias.

Clinical risk stratification was assessed using HbA1c clinical category cut points of <5.7%, 5.7-6.4%, and ≥6.5%. Fisher's exact test was used to assess differences associated with risk.

LINEAR REGRESSION

PTS A1CNow+ system
y = 0.986 (±0.036) x + 0.13 (±0.203)

Clinical Lab analyzers
y = 1.020 (±0.019) x + 0.24 (±0.17)

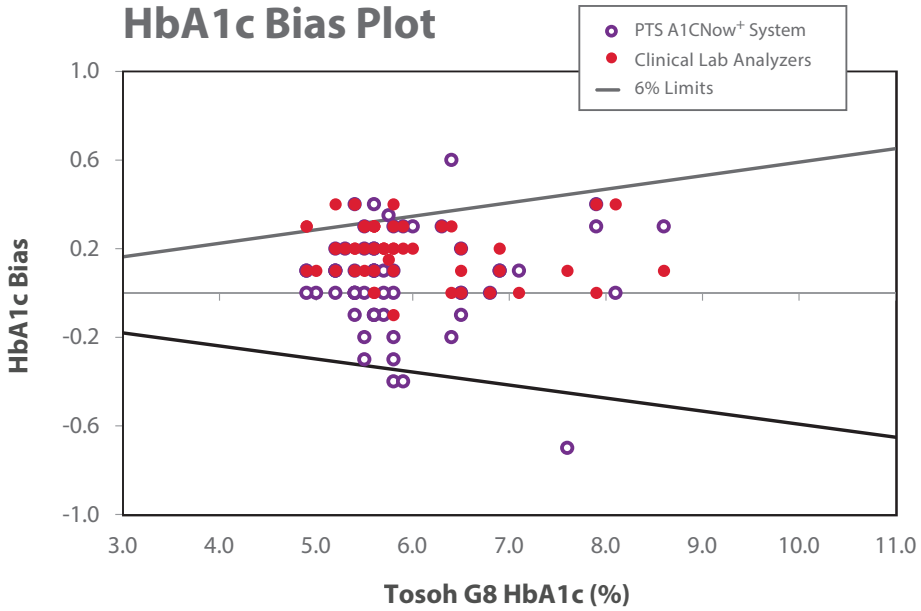


BIAS

Both the A1CNow+ system and CL analyzer results are within acceptable ±6% bias

PTS A1CNow+ system
Average Bias +0.3%

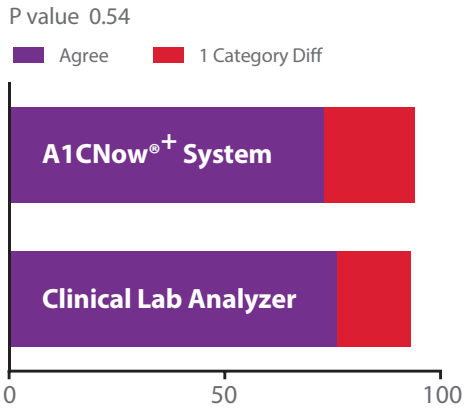
Clinical Lab analyzers
Average Bias +3.8%



CLINICAL RISK

The A1CNow+ system and CL analyzers are both able to accurately assess patient risk.

HbA1c Clinical Risk



Tosoh G8 Risk Stratification

PTS A1CNow+ system
77.7% risk agreement

Clinical Lab analyzers
81.7% risk agreement

RESULTS SUMMARY

In total, slopes were 1.020 and 0.986 for CL and the A1CNow+ system relative to Tosoh ($p = 0.63$); r of 0.99 and 0.96, and intercept 0.24 and 0.13, respectively ($p = 0.64$). Bias was 3.8% for CL analyzers and 0.3% for the A1CNow+ system. Risk classification was unchanged in 81.7% of CL analyzers and 77.7% of A1CNow+ system measurements, resulting in non-statistical ($p = 0.54$) category 1 differences between the POC and CL methods. There were no category 2 risk differences regardless of method.

CONCLUSIONS

Based on the results of this study, the PTS Diagnostics A1CNow+ system is as accurate in measuring HbA1c relative to three clinical laboratory analyzers and well within the ±6% CAP guideline for bias. Risk stratification revealed no differences between the clinical laboratory and A1CNow+ system in classifying the patient state.

Ease of use and disposability of the A1CNow+ system provides an advantage in measuring HbA1c in situations where clinical laboratory analyzers are unavailable to provide physicians with real-time information to better manage diabetes.

[1] PTS Diagnostics, 7736 Zionsville Road, Indianapolis, IN 46268
[2] Dominican Hospital – Dignity Health, 1555 Soquel Drive, Santa Cruz, CA 95065
[3] Kaiser, 11000 East 45th Avenue, Denver, Colorado 80239

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PTS Diagnostics A1CNow®+: A Valuable Tool in a Value-Based World

Carrie Jo Szablowski, MLS(ASCP); Kaddy Davis; James H. Anderson, MD

PTS Diagnostics, Indianapolis, IN

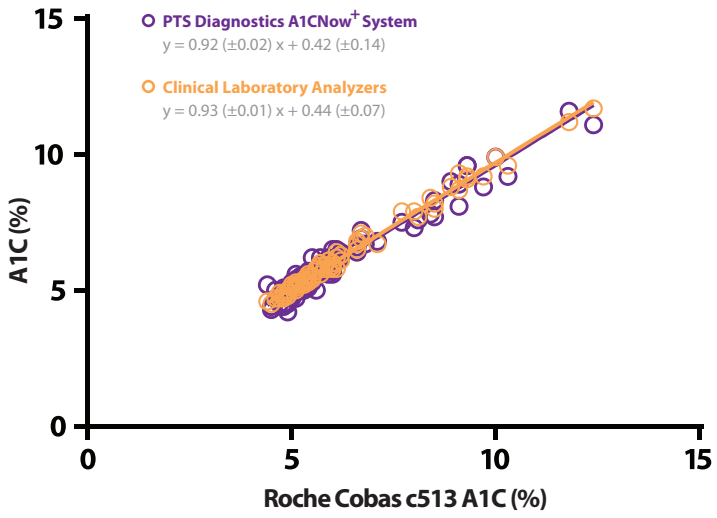
BACKGROUND

Value-based medicine is a new healthcare model to shift physician focus from the quantity of services and revenue generated to quality and value of healthcare provided. The basis for this model is the idea of the right care for the right patient in the right environment at the right time, also known as Patient Centered Medical Home (PCMH). Point-of-care A1C testing can maximize patient and provider engagement by obtaining the results in real-time which allows for effective communication, healthy discussions, and improved healthcare.
This study evaluated the accuracy of A1CNow+ as a tool to assist with PCMH for diabetes management.

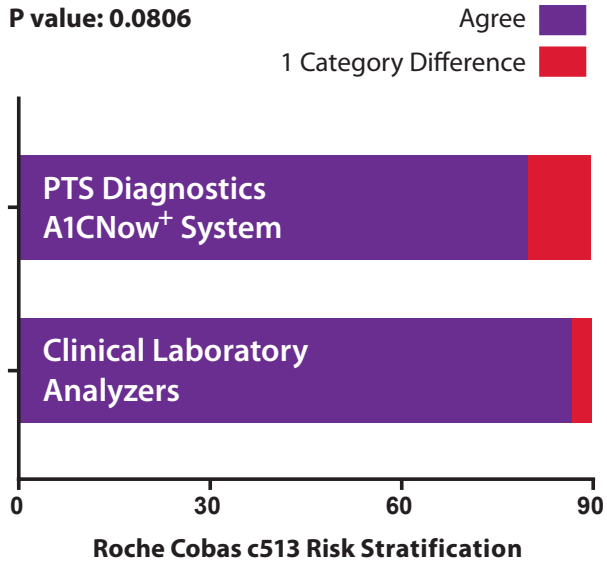
METHODS

Blood was collected from PTS employees. A1C values ranged from 4.4 - 12.4 %A1C for a total of 90 data points. Capillary blood was tested on the PTS Diagnostics A1CNow+ system while venous blood was tested at PTS Diagnostics on the Tosoh G8 and Roche Cobas® Integra® 400 plus as clinical laboratory comparators. For reference, venous blood was tested at LabCorp on the Roche Cobas c513. Deming regression analysis was used to evaluate accuracy and paired differences to measure bias. Clinical risk was assessed using A1C clinical cut points of < 5.7, 5.7 - 6.4, and ≥ 6.5 %A1C. Fisher's exact test was used to assess differences amongst methods.

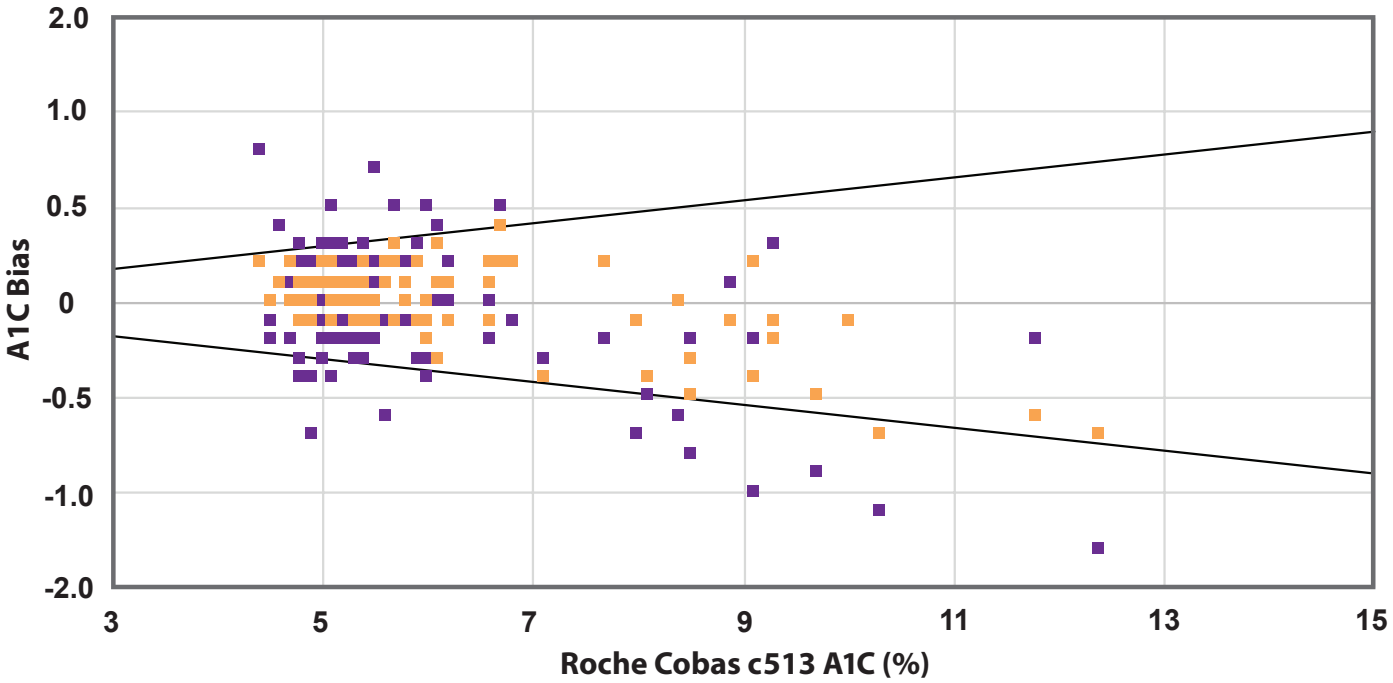
A1C DEMING REGRESSION



A1C CLINICAL RISK



A1C BIAS PLOT



■ **PTS Diagnostics A1CNow+ System**
Average Bias -0.83%

■ **Clinical Laboratory Analyzers**
Average Bias +0.17%

RESULTS

Average paired percent bias was -0.83% for the A1CNow+ and +0.17% for the clinical laboratory analyzers. Slopes were 0.92 and 0.93 (p=0.35) and intercepts were 0.42 and 0.44 (p=0.098) for the A1CNow+ and clinical laboratory, respectively. Clinical risk agreement was 89% for A1CNow+ and 97% for clinical laboratory analyzers (p=0.08).

CONCLUSION

The A1CNow+ was shown to be as accurate as the clinical laboratory in measuring A1C. Risk analysis showed no statistical difference between the clinical laboratory and A1CNow+ in classifying A1C clinical cut points. The A1CNow+ is a valuable tool to help meet the goals of the Quadruple Aim which seeks to improve the health of the population, improve the patient experience of care, improve the provider experience of giving care, and reduce the cost of healthcare in a value-based world.

Carrie Jo Szablowski, MLS (ASCP)CM
Director of Global Clinical and Technical Support

cszablowski@ptsdiagnostics.com
p +1 (317) 870-5610 ext. 1129
7736 Zionsville Road
Indianapolis, IN 46268 / USA

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A1CNow®+ System

Precision and Comparison Study Summary

1 PROTOCOL

This evaluation was conducted in June 2020. It consisted of precision testing and a comparative analysis of the A1CNow®+ system. The study compared fingerstick samples on the A1CNow+ system to venous whole blood samples tested on the NGSP Level II Laboratory Certified Tosoh G8 (Tosoh G8) at PTS Diagnostics, Sunnyvale, CA and on a Roche Cobas analyzer at a LabCorp reference laboratory (Roche Cobas). A total of twenty (20) subjects were tested.

At the test site, a PTS Diagnostics employee performed a venipuncture blood draw and collected one (1) EDTA whole blood lavender top tube and one (1) lithium heparin whole blood green top tube from each subject. An additional lithium heparin whole blood tube was drawn from three (3) subjects and retained in the testing area for use in the precision study. The lithium heparin tube from each subject was placed in a cooler with ice packs and shipped via overnight courier to PTS Diagnostics in Sunnyvale, CA for next day delivery for HbA1c analysis on the Tosoh G8. The EDTA tube from each subject was placed in a cooler with ice packs and transported to LabCorp for analysis on a Roche Cobas analyzer.

After the venipuncture, a PTS Diagnostics employee performed a fingerstick on each subject. A 5µL blood sample was collected for the A1CNow+ system using the blood collector provided in the kit and analyzed according to the instructions for use.

The precision study was performed using the whole blood collected in the lithium heparin tubes. Three samples, one each, with low, mid, and high values for HbA1c were run ten (10) times each on a single A1CNow+ system.

All samples tested for HbA1c were within the claimed measuring range of the analyzers used.

2 RESULTS

Evaluation by Average Difference

The following graphs and tables show the detailed analyses of the relationship of the results from the A1CNow+ System, the PTS Diagnostics Tosoh G8 and the LabCorp Roche Cobas analyzer.

The difference between the A1CNow+ result and the laboratory result is calculated pair-wise. The average of the differences is calculated.

The average differences (bias) were calculated from the individual paired % Bias results to the **Tosoh G8** analyzer (Table 2.1).
%Bias Roche to Tosoh = ((**Roche Cobas result** – Tosoh G8 Lab Result) ÷ Tosoh G8 Lab result) * 100
%Bias A1CNow+ to Tosoh= ((**A1CNow+ result** – Tosoh G8 Lab Result) ÷ Tosoh G8 Lab Result) * 100:
:

Table 2.1 Average % Bias vs. Tosoh G8

	Roche Cobas	A1CNow+ System
HbA1c (%)	-0.1%	-0.8%

The average difference (bias) was calculated from the individual paired % Bias to the **Roche Cobas** analyzer (Table 2.2).
%Bias A1CNow+ to Roche= ((A1CNow+ result – Roche Cobas result) ÷ Roche Cobas result) * 100:

Table 2.2 Average % Bias vs. Roche Cobas

	A1CNow+ System
HbA1c (%)	-0.7%

Analyte Summary

The summary of the linear regression and predicted bias data is shown in Section 3 for HbA1c in Tables 3.1-3.4. This data is then used to calculate the predicted bias at specific clinical decision values spanning the dynamic (measuring) range of the assay on the Tosoh G8. Actual predicted percent differences (bias) with the reference analyzers (Roche Cobas and Tosoh G8) are calculated as:

(A1CNow+ result – Reference method result) ÷ Reference method result * 100 = % Bias

3 HbA1c (%)

Table 3.1 HbA1c (%) vs. Tosoh G8

	Roche Cobas	A1CNow+ System
Number of Replicates (n)	20	20
Slope	1.00	0.97
y-Intercept	0.0	0.1
Correlation Coefficient (r)	0.996	0.960

Table 3.2 HbA1c (%) vs. Roche Cobas

vs. Roche Cobas	A1CNow+ System
Number of Replicates (n)	20
Slope	0.97
y-Intercept	0.2
Correlation Coefficient (r)	0.963

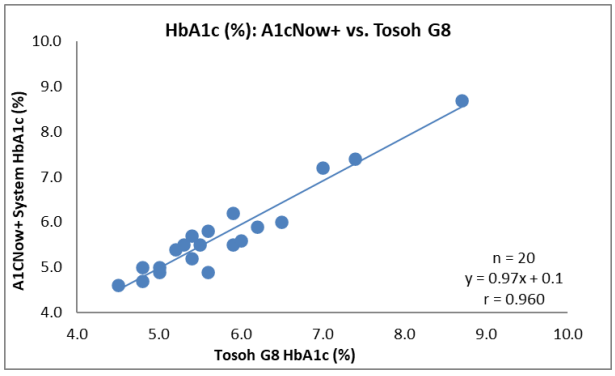
Table 3.3 HbA1c (%) Predicted Bias to Tosoh G8

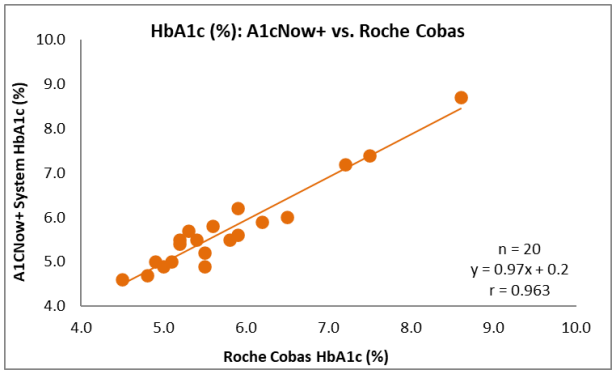
Tosoh G8	Roche Cobas	% Bias	A1CNow+ System	% Bias
4.0	4.0	-0.1%	4.0	0.3%
5.7	5.7	-0.1%	5.7	-0.8%
6.5	6.5	-0.1%	6.4	-1.1%
7.0	7.0	-0.1%	6.9	-1.3%
	Average % Bias	**-0.1%**		**-0.8%**

Table 3.4 HbA1c (%) Predicted Bias to Roche Cobas

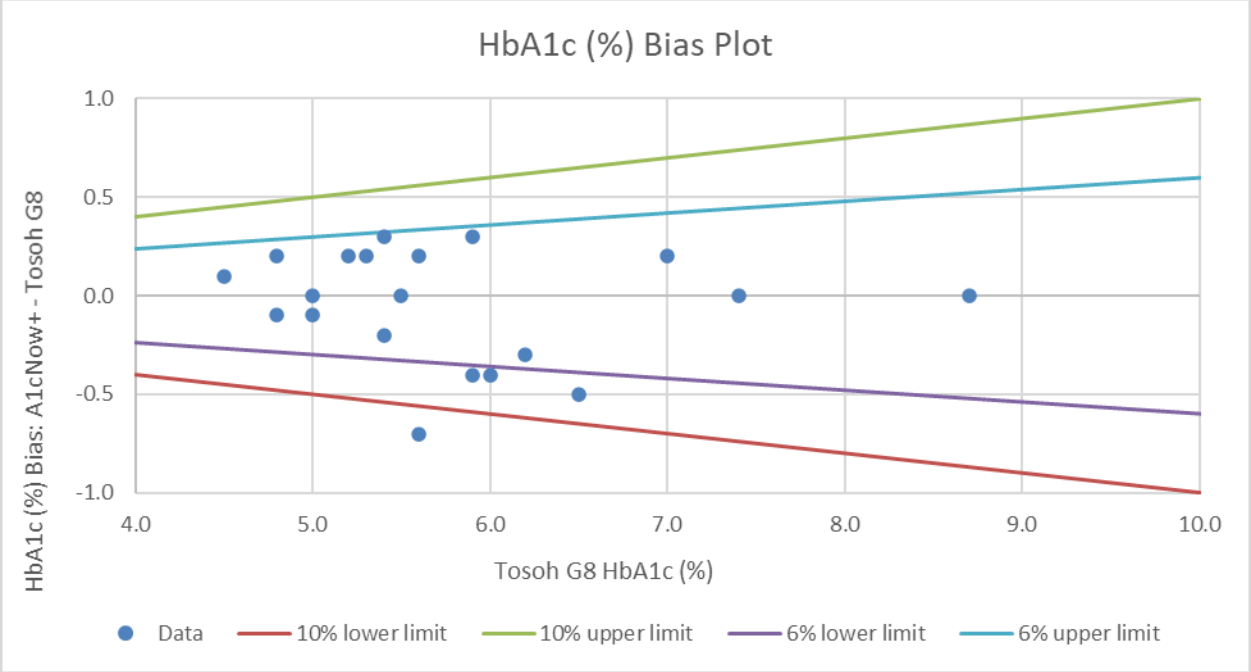
Roche Cobas	A1CNow+ System	% Bias
4.0	4.0	0.4%
5.7	5.7	-0.7%
6.5	6.4	-1.1%
7.0	6.9	-1.2%
	Average % Bias	**-0.7%**

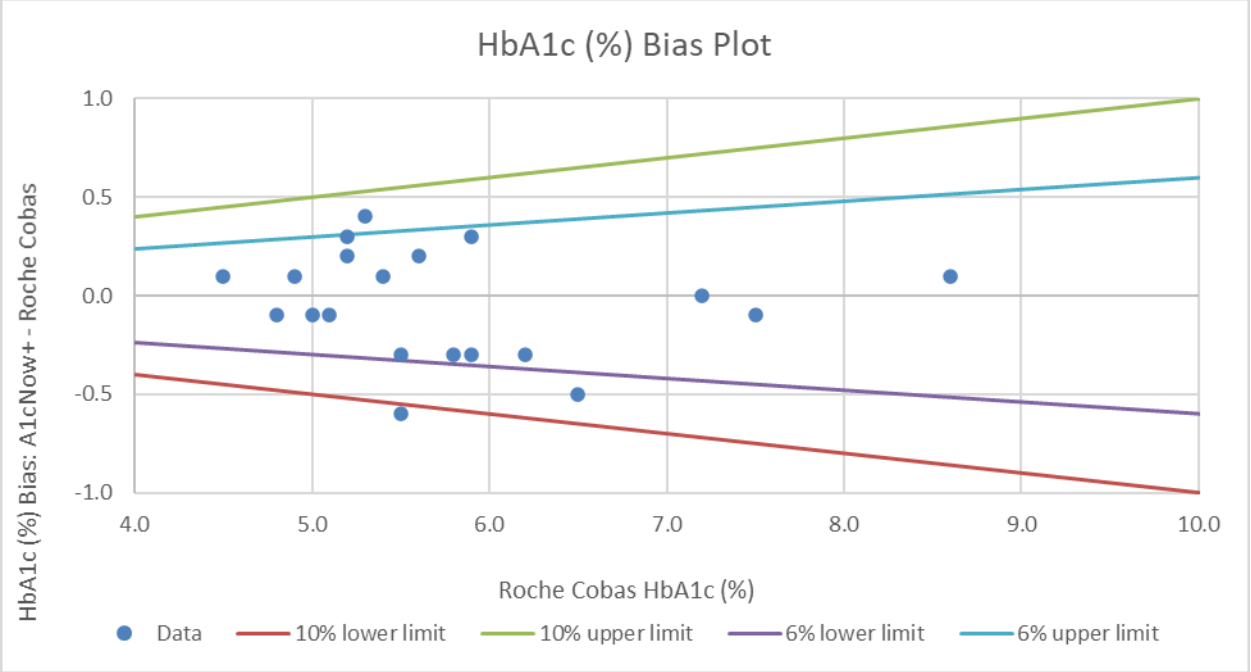
Predicted biases are calculated from the linear regression line of the data collected.





3 HbA1c (%), CONTINUED





4 RISK CLASSIFICATION

Each result was categorized based on traditional risk categories for HbA1c (Table 4.1). From these analyses, clinical agreement tables were compiled (Table 4.2 and Table 4.3) applying strict limits to quantify "Agreement." This means that a sample yielding a HbA1c (%) result of 5.6% for a reference system result of 5.7% was rated as a 1 category difference despite the clinical insignificance of the difference. These results are shown as the number of values where there is clinical agreement (Agree), a one category difference (1 Cat Diff) or a two-category difference (2 Cat Diff) between the A1CNow^{+} system and the reference laboratory result**.** In no instance was a "2 Category Difference" observed in this clinical evaluation for HbA1c.

Table 4.1 **Risk Classification (HbA1c)**

Categories	**HbA1c (%)**		
	<5.7	5.7 – 6.4	≥6.5

Table 4.2 Risk Classification Agreement Between Methods and Tosoh G8

	HbA1c (%)		
	Agree	**1 Cat Diff**	**2 Cat Diff**
Roche Cobas	20	0	0
A1CNow^{+} System	15	5	0

Table 4.3 Risk Classification Agreement Between Methods and Roche Cobas

	HbA1c (%)		
	Agree	**1 Cat Diff**	**2 Cat Diff**
A1CNow^{+} System	15	5	0

5 PRECISION

A1CNow+ System Results (HbA1c %)			
	Sample - Low	**Sample - Medium**	**Sample - High**
1	4.6	6.5	9.3
2	5.1	6.8	7.5
3	5.0	7.1	8.4
4	5.0	7.3	8.0
5	4.9	6.6	8.3
6	4.7	6.5	8.9
7	5.1	7.0	8.9
8	4.8	6.6	8.8
9	4.7	6.8	8.6
10	4.6	6.7	7.7
Number of replicates (n)	10	10	10
Average (HbA1c (%))	4.9	6.8	8.4
Standard Deviation (HbA1c (%))	0.2	0.3	0.6
CV (%)	4.0	4.0	6.8

6 OVERVIEW OF EVALUATION

PTS Diagnostics Technical Support

PTS Technical Support
(317) 870-5610
customerservice@ptsdiagnostics.com

Reference Methods: (X-axis)

PTS Diagnostics – Sunnyvale, CA: NGSP Level II Laboratory Certified Tosoh G8
LabCorp – Dublin, OH: Roche Cobas

Reagents Used: Accuracy and Precision

A1CNow+ System: Lot 2000228, Exp: 08/19/2021
A1CNow+ Controls: Lot 61050A, Exp: 11/30/2022

7 REGRESSION STATISTICS SUMMARY

Statistical Definitions

Slope: The slope of a line in the plane containing the *x* and *y* axes is generally represented by the letter *m*, and is defined as the change in the *y* coordinate divided by the corresponding change in the *x* coordinate, between two distinct points on the line. (A perfect slope is "1")

Intercept: Where a straight line crosses the Y-axis of a graph. (A perfect intercept is "0")

Correlation Coefficient (r Value): A statistic that gives a measure of how closely two variables are related, also known as the correlation coefficient. It represents the extent to which variations in one variable are related to variations in another or "goodness of fit."

Comparison Key Aspects

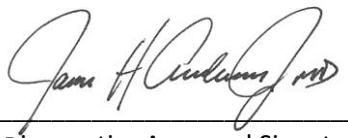
Any method comparison must be approached with a clear understanding of variables that affect the test results. The known variation of chemistry analytical systems must always be considered when evaluating observed bias. Such variation is not only evident between point-of-care testing and laboratory systems but also between laboratory systems. Even in the most closely aligned systems, two methods may "correlate" but rarely "match". Identity is not a prerequisite for acceptance, but rather an understanding of the bias at clinical decision limits for the analyte in question and the clinical consequences of these biases. The critical evaluation criterion is the placement of a given patient into appropriate risk categories by each system. In this analysis, a point-by-point comparison was made for each patient evaluating the risk classification category for each result.

Data Summary (PTS Diagnostics Internal Evaluation)

The A1CNow$^+$ test system in this study produced clinically comparable values for hemoglobin A1c compared to those reported for the same patient samples analyzed on the NGSP Level II Laboratory Certified Tosoh G8 (Tosoh G8) at PTS Diagnostics, Sunnyvale, CA and on a LabCorp Roche Cobas (Roche Cobas). The linear regression results between the methods indicate a good correlation between the A1CNow$^+$ analyzer point-of-care method and the reference laboratory methods for hemoglobin A1C. The risk classification tables demonstrate that the A1CNow$^+$ analyzer accurately identifies patient risk category with a high level of correlation with reference methods.

James H. Anderson Jr., MD, FFPM, FACE

Medical Director



PTS Diagnostics Approval Signature

21 May 2021

Date