Glucose Analytical Comparability Evaluation of the YSI 2300 STAT Plus™ and YSI 2900D Biochemistry Analyzers

YSI Life Sciences
White Paper B91

Authors: Kevin Schlueter, PhD, Jay Johnson, PhD, Christopher Warner and William Miller

ABSTRACT

BACKGROUND

The YSI 2300 STAT Plus Glucose and Lactate Analyzer (YSI 2300) is a Class II in-vitro diagnostics (IVD) medical device, which is widely accepted as a method for reference measurements and system calibration by most manufacturers of blood glucose (BG) monitoring systems. YSI has developed a new generation analyzer, the YSI 2900D Biochemistry Analyzer (YSI 2900), employing the same biosensor technology as the YSI 2300, but is a non-IVD analyzer. As new systems must demonstrate high-quality analytical performance, a comparative study was conducted with the YSI 2900 and YSI 2300 to evaluate their precision and accuracy for human whole blood (WB) and plasma.

METHODS

To assess validity and reliability, 288 human WB and 288 plasma samples, across a range of values, were analyzed using two analyzers of each YSI model. Non-pooled samples from six lots of human blood from a local blood bank were used for the study.

WB and plasma comparability studies included linear regression, correlation, bias, Medical Decision Point (MDP) and error grid analysis. Within-run precision of glucose and human blood controls was performed as well. All analyzers were tested across a wide glucose range (0.0– 750 mg/dl).

RESULTS

Linear regression analysis for paired YSI 2900 and YSI 2300 results showed high correlation ($R \geq 0.99$) and similar regression statistics for both WB and plasma. Within-run precision testing with both systems produced coefficients of variation (CVs) of <2% for all sample types and glucose levels. Consensus and Clark and consensus error grid analysis showed equivalent clinical accuracy with 100.0% (238/238) of WB results and 100.0% (288/288) of plasma results within zone A. The YSI 2900 analyzer met all MDP criteria.

CONCLUSION

The YSI 2900 analyzer was comparable to the YSI 2300 analyzer, providing fast, reliable measurements of whole blood and plasma glucose concentrations over a wide range of values.

INTRODUCTION

The YSI 2300 is a Class II IVD medical device designed for clinical diagnostics and sports physiology applications. Today, the YSI 2300 analyzer is widely accepted as a method for reference measurements and system calibration by most of the manufacturers of BG monitoring systems.

The YSI 2900 is a laboratory instrument intended for use in research, biotechnology and food-processing applications. Not indicated for human medical diagnostic use, this new generation analyzer has been increasingly adopted as a reference standard by BG manufacturers, as it uses the same biosensor technology as the YSI 2300. Therefore, the aim of this study was to demonstrate equivalence of the YSI 2300 and YSI 2900 analyzers concerning glucose analytical performance using reference standards, human WB, and human plasma samples.

MATERIALS AND METHODS

YSI 2300 AND YSI 2900 ANALYZERS

Both YSI 2300 and YSI 2900 analyzers (YSI, Inc., Yellow Springs, OH USA) employed an enzyme-based, amperometric biosensor for measuring glucose concentrations. The biosensor used a glucose oxidase-containing membrane for oxidizing glucose to gluconolactone and hydrogen peroxide. The hydrogen peroxide was oxidized at the platinum anode, producing electrons. The electron flow was linearly proportional to the steady state hydrogen peroxide concentration and, therefore, to the concentration of glucose. Analysis time was approximately 60 seconds/sample.

Two YSI 2300 and two YSI 2900 instruments were compared side-by-side. Each YSI analyzer was configured with the same calibration and analysis parameters, using the YSI 2300 "5/15" and "Normal Mode" of operation (1, 2). The calibration point was set at 180 mg/dl. Samples were analyzed on both probes of each analyzer. Analyzer probes were designated as A or B and B or W, for the YSI 2900 and YSI 2300, respectively. All analyzers used the same lot of glucose oxidase membranes. Membrane replacement was not conducted during this study.

DAILY MEMBRANE AND LINEARITY CHECKS

Daily membrane integrity and linearity checks were performed prior to conducting WB and plasma sample analyses using YSI protocols (1,2). Each biosensor membrane was tested for structural integrity against YSI 2363 Potassium Ferrocyanide (KCN) solution (YSI, Inc., Yellow Springs, OH USA). YSI 1531 Glucose Linearity Standard, 9.00 g/L (YSI, Inc., Yellow Springs, OH USA), was used for the daily linearity testing.

WB AND PLASMA ANALYSIS

WB human blood samples were obtained from the Dayton Community Blood Center (DCBC) (Dayton, OH USA). Samples were drawn from volunteer community donors and collected in 5 ml Vacutainer® tubes containing EDTA (Becton-Dickinson, Franklin Lakes, NJ USA). The WB samples were refrigerated at DCBC for 7 days and then transported to the YSI site under refrigerated conditions. YSI was blinded to all donor characteristics (name, gender, age, race, health, etc.). Hematocrit values were not forwarded with the samples.

Prior to conducting the experiments, WB glucose levels were analyzed on a YSI 2300 to verify sample glucose concentrations. The glucose levels were expected to be at 0 mg/dl due to metabolic glucose consumption by live blood cells. This was found to be true on all unspiked samples tested.

The WB samples were subsequently removed from refrigeration and spiked with a known concentration of glucose. The glucose spiking solution concentration was 200.0 mg/ml and made using a standard protocol (3). Assuming an average initial blood volume of 4.0 ml, spiking aliquot volumes were calculated to ensure glucose levels spanned the analytical range of the instruments. After spiking, the samples were mixed and equilibrated on a rocker for 20 – 30 minutes. After equilibration all WB samples from each set were analyzed on each YSI instrument. No more than 5 minutes was allowed to elapse between each instrument analyses.

Once each WB sample set analysis was completed, tubes with remaining WB were centrifuged in a refrigerated tabletop centrifuge at 3000 X G RCF for 15 minutes. Each sample tube's supernatant plasmas were transferred to corresponding labeled tubes for subsequent plasma analysis. Plasma analysis was conducted in the same manner as the WB samples.

At the close of the study all blood and plasma samples were disposed of by an authorized medical biohazard waste service.

WITHIN-RUN PRECISION

The within-run precision evaluation was conducted using a YSI glucose standard and a whole blood glucose control. Forty replicates of YSI 2715 Glucose Standard, 400 mg/dl, (YSI, Inc., Yellow Springs, OH USA) were run on each analyzer. YSI 2715 is a NIST-traceable glucose standard.

Bio-Rad Meter Trax™ Trilevel human blood glucose controls (Bio-Rad Laboratories, Irvine, CA USA) were used for the whole blood precision evaluation. The control kit consisted of low, mid and high glucose concentrations as specified by

the manufacturer (4). The Bio-Rad controls were refrigerated and prepared per the manufacturer's recommendations prior to analysis (4). Blood glucose precision tests were performed in replicates of seven samples for each analyzer.

The coefficient of variation (CV) was calculated for the YSI and blood glucose precision tests.

ANALYZER ACCURACY

Six sets of 8 WB and plasma samples were analyzed over a 6-day period, with each set analyzed on its own respective day. All samples were run in triplicate for each probe, providing a total of six analyses per sample. Thus, a total of 288 WB and 288 plasma analyses were used for the linear regression, bias and MDP evaluations.

The paired results from the YSI 2300 and YSI 2900 analyzers were plotted against each other using Data Innovations EP Evaluator® software (S. Burlington, VT USA) for regression, bias and MDP analysis. Deming regression analysis was chosen based on the assumption that both analyzer models were subject to measurement error and that the analytical methods were essentially identical (5). The correlation between YSI model results were analyzed using linear regression analysis.

MDP's were set at 45 mg/dl, 100 mg/dl, 126 mg/dl and 180 mg/dl based on the prescribed guidelines set by the American Diabetes Association and Statland (6,7). MDP's were calculated by the EP Evaluator software application using Deming linear regression.

Clinical accuracy was evaluated using consensus (Parkes) and Clark error grid analysis, which categorizes analyzer results according to the degree of clinical risk posed by an inaccurate measurement (8,9). Data Innovations EP Evaluator software was used to analyze the data.

RESULTS AND DISCUSSION

DAILY MEMBRANE & LINEARITY CHECKS

All instruments utilized for the study were required to pass daily performance checks prior to analyzing samples. For acceptable glucose oxidase membrane integrity, a FCN test value of ≤ 5 mg/dl is required. FCN values for all membranes were well below 5 mg/d, indicating structurally intact membranes.

The acceptable range for the 9.00 g/L glucose linearity standard was 8.55 – 9.45 g/L, which is ± 5% of the linearity check point. All instruments met the linearity specifications for each day of testing.

WITHIN-RUN PRECISION

The YSI 2300 and YSI 2900 analyzers demonstrated similar within-run precision for both the YSI glucose standard and Bio-Rad blood glucose controls. The CVs for each system were below 2%, which met YSI's CV specification of ≤ 2% (*Table 1*).

Table 1: Summary of Within-run Precision

Sample	Target glucose (mg/dl)	YSI 2300-A CV (%)	YSI 2300-B CV (%)	YSI 2900-A CV (%)	YSI 2900-B CV (%)
YSI Glucose Standard	400 ± 20	1.21	1.44	1.81	1.87
Bio-Rad Low Control	77 ± 32	0.44	1.53	1.00	0.45
Bio-Rad Mid Control	153 ± 49	0.54	1.36	1.57	0.94
Bio-Rad High Control	363 ± 102	0.64*	0.74	1.64	1.73

*n=4 due to limited sample availability

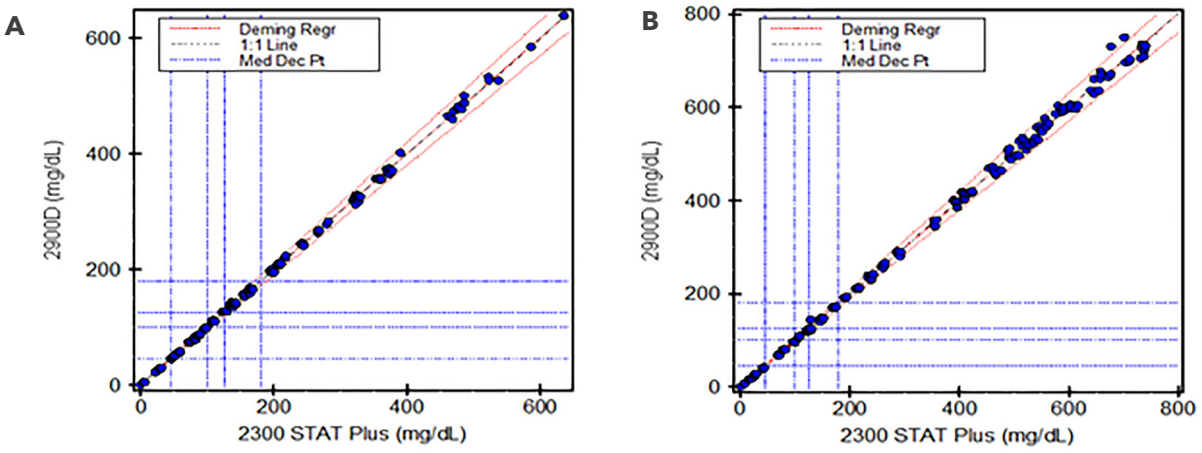

Figure 1: Deming regression analysis of glucose in WB (A) and Plasma (B) obtained with the YSI 2900 versus the YSI 2300. Vertical and horizontal dotted lines represent MDP's (45 mg/dl, 100 mg/dl, 126 mg/dl and 180 mg/dl).

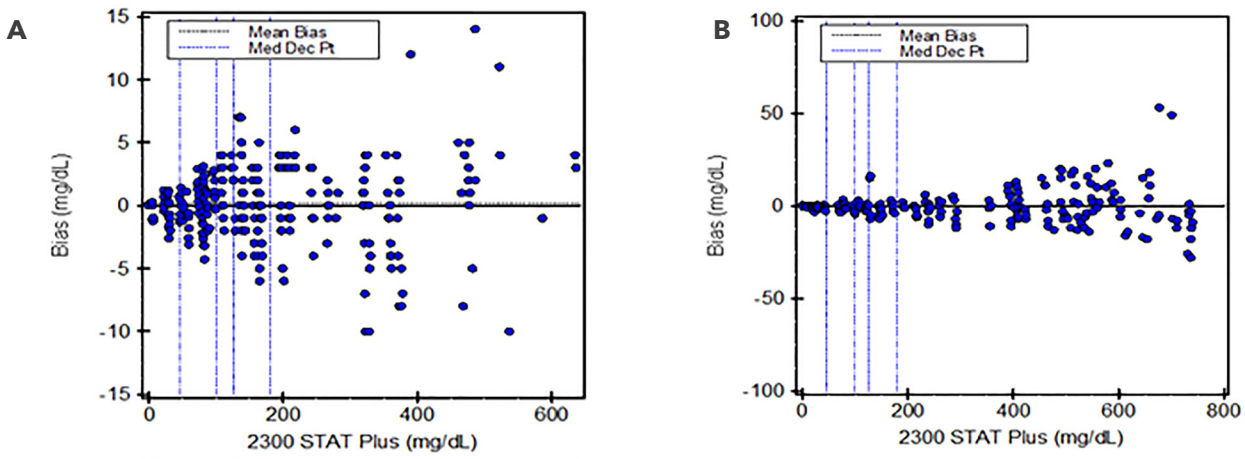

Figure 2. Measurement bias of glucose in WB (A) and Plasma (B) obtained with the YSI 2900 versus the YSI 2300. Vertical dotted lines represent MDP's (45 mg/dl, 100 mg/dl, 126 mg/dl and 180 mg/dl).

REGRESSION ANALYSIS AND BIAS

A total of 288 WB and 288 plasma samples, representing a wide range of blood glucose concentrations (WB: 0.0 – 650 mg/dl, plasma: 0.0 – 750 mg/dl), were analyzed for Deming linear regression and bias. Scatter plot bounds were set at 5.0% total allowable error.

Linear regression analyses for paired YSI 2900 and YSI 2300 results showed high correlation (R ≥ 0.99) and similar regression statistics for both WB and plasma (Figure 1 and Table 2). The 95% confidence intervals for both slope and intercept contained the values of 1.00 and 0.00, respectively, further indicating statistical equivalence.

Table 2: Regression Analysis

	Whole Blood	Plasma
Slope	1.001 (0.998 to 1.004)	1.002 (0.998 to 1.006)
Intercept	-0.0029 (-0.5791 to 0.5849)	-1.1437 (-2.5193 to 0.2320)
Correlation Coefficient (R)	0.9997	0.9994
95% Confidence Intervals are shown in parentheses		

Bias for both WB and plasma were evenly distributed around the zero line (Figure 2). Mean percent bias was low for YSI 2900 WB (0.1%) and plasma (−0.2%).

MEDICAL DECISION POINT ANALYSIS

A MDP is an analyte concentration at which medical decisions change. If the concentration is to one side of the MDP, one decision is made; if on the other side of the MDP, a different decision is made (5). Therefore, it is particularly important that both the YSI 2300 and YSI 2900 agree at the MDPs. Both analyzers are considered statistically identical when the 95% Confidence Interval for each YSI 2900 MDP includes the corresponding YSI 2300 MDP. MDP analysis for WB and plasma are shown in Tables 3 and 4, respectively. Comparison of the MDP's showed a high degree of correlation between the instruments.

Table 3: Medical Decision Point Analysis of WB Samples

YSI 2300	YSI 2900	95% Confidence Limit	
MDP	Predicted MDP	low	High
45	45.0	44.5	45.5
100	100.1	99.7	100.5
126	126.1	125.7	126.5
180	180.2	179.8	180.5

Table 4: Medical Decision Point Analysis of Plasma Samples

YSI 2300	YSI 2900	95% Confidence Limit	
MDP	Predicted MDP	low	High
45	44.0	42.7	45.2
100	99.1	98.0	100.2
126	125.2	124.1	126.2
180	179.3	178.3	180.3

ERROR GRID ANALYSIS

Consensus and Clark error grid analysis of YSI 2300 (reference method) and YSI 2900 (alternate method) WB and plasma samples were conducted within the analytical range of 0.0 – 550.0 mg/dl. Mean % error for WB and plasma was 1.8% and 2.5%, respectively. Both error grids demonstrated analytical comparability and clinical accuracy as 100% (288/288) of WB and 100% (238/238) of plasma results were located in zone A (*Figures 3 and 4, Table 5*).

Table 5: Number and Percentage of Results within Consensus Error Grid

Sample Type	Zone A	Zone B	Zones C, D & E
Whole Blood	288/288	0/288	0/288
	(100.0%)	(0.0%)	(0.0%)
Plasma	238/238	0/238	0/238
	(100.0%)	(0.0%)	(0.0%)

Zone A = no effect on clinical action (clinically accurate);
Zone B = altered clinical action – little or no effect on clinical outcome;
Zone C = altered clinical action – likely to affect clinical outcome;
Zone D = altered clinical action – could have significant medical effect;
Zone E = altered clinical action – could have dangerous consequences

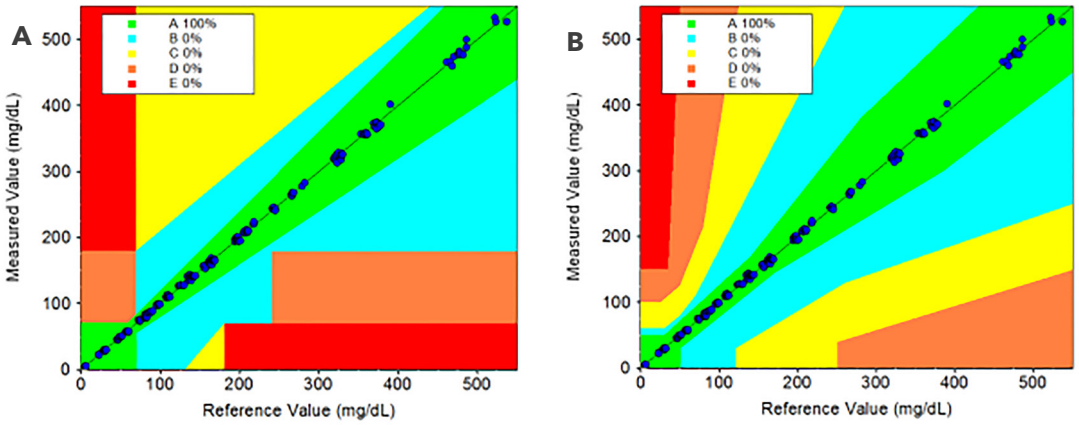

Figure 3. Clinical significance inaccuracy measurements of YSI 2900 WB samples by Clarke (A) and Consensus (B) Error Grid analysis. The reference value represents the YSI 2300 method. The measured value represents the YSI 2900 method.

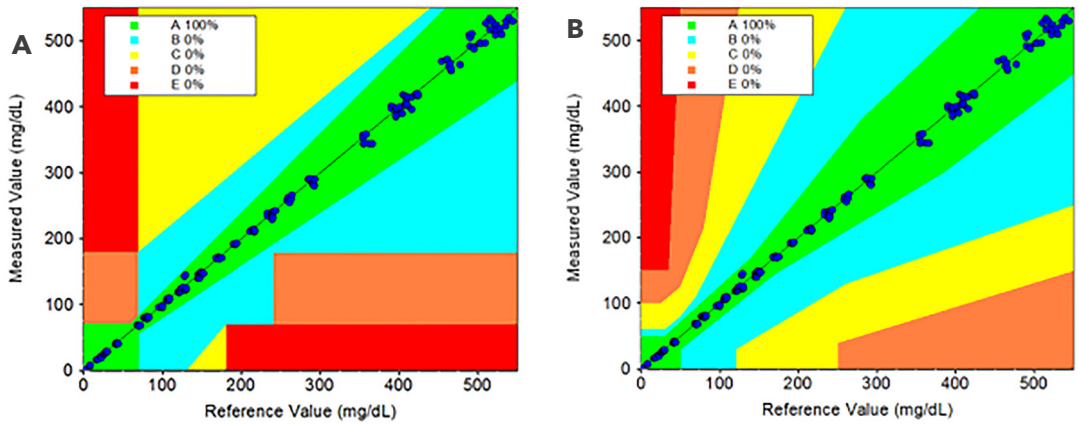

Figure 4. Clinical significance inaccuracy measurements of YSI 2900 plasma samples by Clarke (A) and Consensus (B) Error Grid analysis. The reference value represents the YSI 2300 method. The measured value represents the YSI 2900 method.

CONCLUSIONS

Data collected on the YSI 2900 analyzers indicate that the analyzer provides precise and accurate whole blood and plasma glucose readings across a wide range of blood glucose concentrations. Based on results of this study, the YSI 2900 demonstrated analytical comparability to that of the YSI 2300.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge the contributions of Gerry Pitts, who assisted with the analyzer preparation and sample analysis, and Barry Uffindell for his technical assistance.

REFERENCES

1. *User's Manual for YSI 2300 STAT Plus™ Glucose and Lactate Analyzer. 2009. https://www.ysi.com/File%20Library/Documents/Manuals/YSI-2300-Stat-Plus-manual-j.pdf*
2. *User's Manual for YSI 2900D Analyzer. 2016. https://www.ysi.com/ysi-2900-nutrient-biochemistry-analyzer*
3. *ACCU-CHECK® and AccuData® Systems Evaluation Protocol. Glucose Spiking Protocol for Glucose Meter Evaluations. Roche Diagnostics. 2012.*
4. *Bio-Rad Meter Trax™ Trilevel Control: Low, Mid and High Package Insert. Bio-Rad Laboratories. 2017.*
5. *Rhoads DG. Lab Statistics, A Practical Approach to Method Evaluation. Fifth Edition: South Burlington, VT; Data Innovations, 2012.*
6. *American Diabetes Association. Classification and Diagnosis of Diabetes. Diabetes Care. 2015 Jan; 38(Supplement 1): S8-S16.*
7. *Statland BE. Clinical Decision Levels for Laboratory Tests, Second Edition: Oradell NJ; Medical Economics Books, 1987.*
8. *Clarke WL, Cox D, Goder-Frederick LA, Carter W, Pohl SL. Evaluating clinical accuracy of systems for self-monitoring of blood glucose. Diabetes Care. 1987;10(5):622-8.*
9. *Parkes JL, Slatin SL, Pardo S, Ginsberg BH. A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. Diabetes Care. 2000;23(8):1143-8.*
10. *CLIA proficiency testing criteria for acceptable analytical performance: Federal Register 1992 Feb 28; 57(40):7002-186*
11. *International Conference on Harmonization (ICH), Guideline for Good Clinical Practice: Consolidated Guidance (E6). FDA. 1996.*
12. *Krouwer JS, Cembrowski GS. A Review of Standards and Statistics Used to Describe Blood Glucose Monitor Performance. Journal of Diabetes Science and Technology. 2010;4(1):75-83.*
13. *CLSI. Measurement Procedure Comparison and Bias Estimation Using Patient Sample; Approved Guideline, Third Edition. CLSI Document EP09-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.*

YSI a xylem brand

Life Sciences
Data for Life.™

YSI Life Sciences develops and manufactures scientific instruments, sensors and systems that serve a variety of scientific and industrial markets worldwide. YSI has a long history in the life sciences and bioanalytical markets, most notably with our introduction of the world's first commercial whole blood glucose analyzer in 1975. Today there are over 10,000 YSI instruments installed around the world, trusted in critical situations to provide the most accurate data in the shortest time.

YSI Inc. | 1725 Brannum Lane | Yellow Springs, OH 45387

Tel +1.937.767.7241 | 800.897.4151 | info@ysi.com | YSI.com/lifesciences

YSI a xylem brand

Life Sciences
Data for Life.™