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White Paper

Glucose analysis comparability evaluation of the YSI 2900C Biochemistry Analyzer to the legacy 2300 STAT Plus™

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Abstract

Background

The YSI 2300 STAT Plus™ (YSI 2300) D-glucose (glucose) and Lactate Analyzer 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 2900C Biochemistry Analyzer (YSI 2900C), employing the same biosensor technology as the YSI 2300, but with updated usability features and form factor. A comparative study was performed to evaluate the accuracy and precision of the new YSI 2900C platform for whole blood (WB), plasma, and serum.

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Methods
To assess comparability and analytical performance, blood samples were taken from volunteers by an on-site phlebotomist. All samples were tested within a 4-hour period from the blood draw event. The analysis was made on whole blood (WB), plasma and serum on three YSI 2300 units, as well as three YSI 2900C units. All units tested glucose over a range of glucose levels and hematocrit (% red blood cells in WB).

Results
Linear regression analysis for paired YSI 2900C and YSI 2300 results showed high correlation ($r \geq 0.999$) and similar regression statistics for venous WB, plasma and serum. Within-run precision testing with both systems produced coefficients of variation (CV) of < 2% for all sample types and glucose levels. Parkes (Consensus) and surveillance EGA (error grid analysis) showed equivalent clinical accuracy with 99.1% (642/648) of WB results, 99.7% (580/582) of plasma results and 99.7% (586/588) of serum results within zone A. Very few points outside zone A were all in zone B (low risk). Surveillance EGA for capillary WB has also 97.7% of results in zone A and all the rest in zone B. The YSI 2900C analyzer met all MDP (medical decision points) criteria.

Conclusion
YSI 2900C exhibited/showed similar performance to the YSI 2300 across all testing matrices: Venous WB, Plasma and Serum.

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 manufacturers of BG monitoring systems.

The YSI 2900D is a laboratory instrument intended for use in research, biotechnology and food-processing applications. The YSI 2900C is an In Vitro Diagnostic Device that is a direct replacement for the YSI 2300. The aim of this study was to demonstrate equivalence of the YSI 2300 and YSI 2900C analyzers concerning glucose analytical performance using human WB, plasma, and serum samples.

Materials and Methods

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

Output from each YSI 2300 probe was aligned with a paired probe on a YSI 2900C of the same membrane lot to create the data pairs.

Whole Blood (WB), plasma and serum analysis

After three instrument pairs were qualified by daily checks, donor subject blood draws initiated. Subjects had been previously recruited and the specimens collected under external IRB constraints and oversight to protect their rights, safety, and well-being. The agency providing this ethical oversight was Advarra IRB, Columbia, MD. All specimens were collected, handled, and stored according to the CLSI guidelines GP41, 7th Edition, "Collection of Diagnostic Venous Blood Specimens". All samples were immediately stored in ice water or refrigerated at 4°C when not in direct use. All testing occurred within four hours of sample collection to minimize preanalytical variability caused by glycolysis during storage. Each WB, PL, or serum sample was tested on the analyzers as close in time as possible. During venous WB testing the test matrix mode selection was set to "Whole Blood" in the instrument set-up control panel. During testing of plasma and serum the mode selection was set to "Plasma". Instrument calibration was performed immediately prior to sampling. Each analyzer has two probes and both probes have glucose sensing membranes. One calibrator lot was used for all instruments and samples in this report. At the conclusion of the study all bloodrelated samples were disposed of by an authorized medical biohazard waste service.

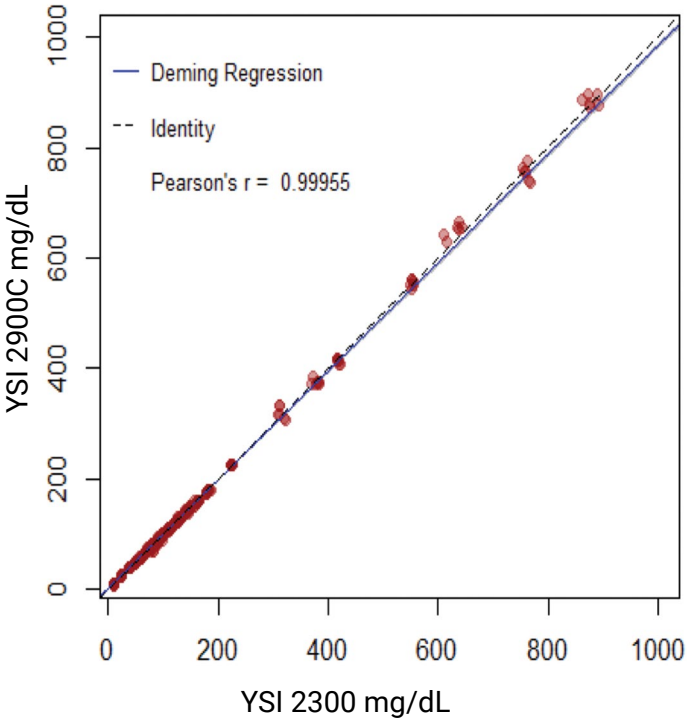
Results and discussion

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 Ferrocyanide (FCN) test value of ≤ 5 mg/dL apparent glucose is required. FCN values for all membranes were well below 5 mg/dL, indicating structurally intact membranes. The acceptable range for the 900 mg/dL glucose linearity standard is 855 - 945 mg/dL, which is ± 5% of the linearity check point. All instruments met the linearity specifications for each day of testing.

Data

The data presented here is a glucose assay from whole blood. Similar data was collected for plasma, serum, and fingerstick capillary whole blood. These were assayed in both the YSI 2300 and the YSI 2900C. In both simulated and actual data sets, the x-axis is always considered the reference assay (output from the predicate device YSI 2300) and the y-axis is always considered the blood glucose monitoring system (output from the YSI 2900C).



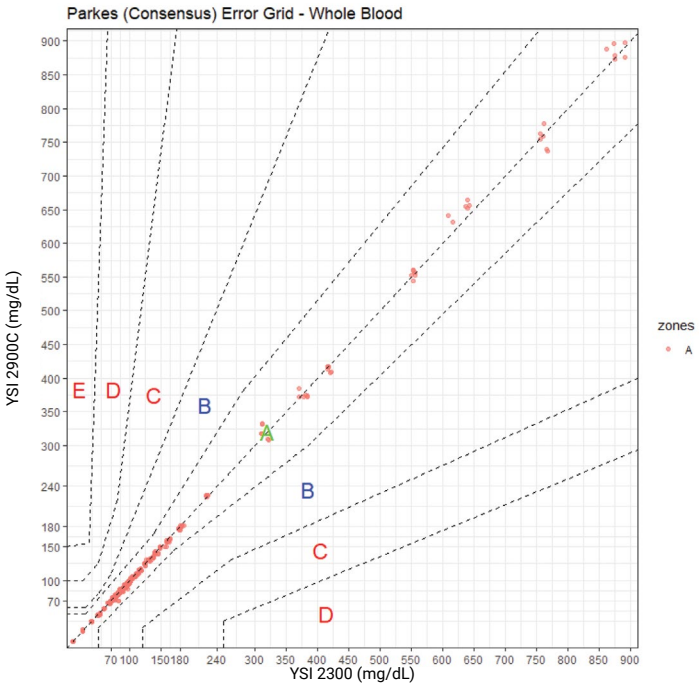
Method comparison - whole blood

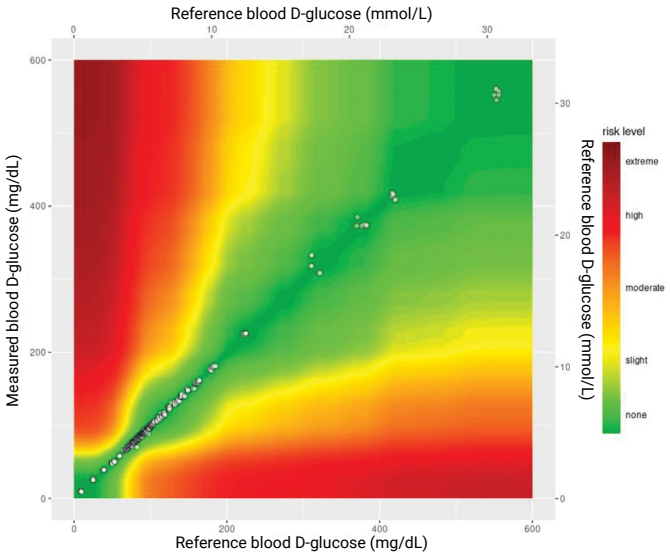
Plot 1. Data pairs over the whole range of D-glucose values tested in whole blood.

A ($1/X^2$) Weighted Deming fit was used as the regression model. The weighting was used to compensate for leveraged bias due to the increasing variance (heteroscedasticity) over the range of the data. The shaded area around the regression line shows the 95% confidence interval (CI) around the slope and intercept of the model. The bootstrap technique was used to calculate the CI. Data are from 111 unique clinical samples.

Data pairs are (YSI 2300, YSI 2900C) in mg/dL Glucose.

Experimental Data-Whole Blood





Data points above 450 or below 50 mg/dL were not available in the native samples. These samples were contrived by spiking or dilution.

	ID	Risk Grade	Number of Pairs	Percent	Risk Factor Range
1	1	A	642	99.1%	0 - 0.5
2	2	B	6	0.9%	> 0.5 - 1.5
3	3	C		NA	> 1.5 - 2.5
4	4	D		NA	> 2.5 - 3.5
5	5	E		NA	> 3.5

Plots 2 & 3 . Error grid analyses. Upper left – Parkes* (Consensus) EGA. Upper right – Surveillance EGA**. In the PEG all points are within risk zone A. Bottom – Table of data per risk grade in SEG. The Parkes EGA plot is shown because it covers the range of measured data whereas the SEG is bounded at 600 mg/dL.

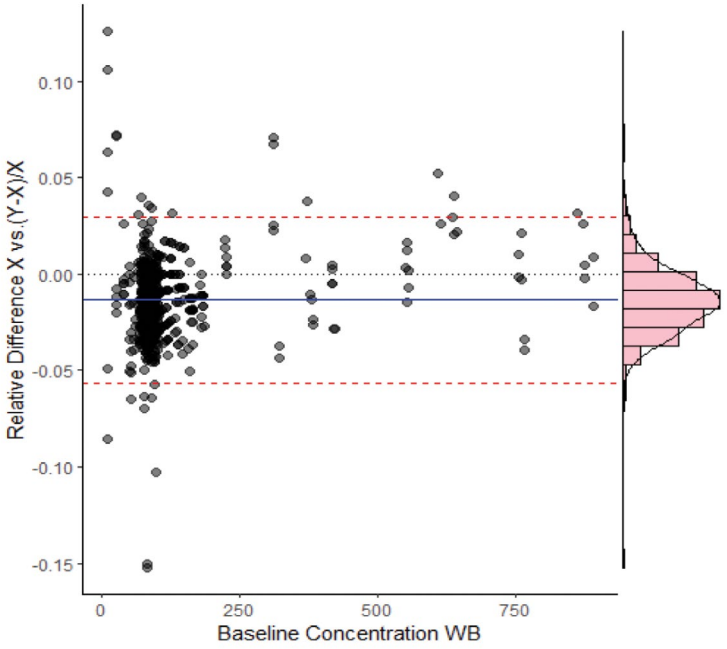
All Parkes EGAs shown are for Type 1 Diabetes.

*Parkes, Joan L., Pardo, Scott, Slatin, Stephen L., and Ginsberg, Barry H., “A New Consensus Error Grid to Evaluate the Clinical Significance of Inaccuracies in the Measurement of Blood Glucose”, Diabetes Care, Vol. 23, No. 8, pp. 1143-1148, August 2000.

**Klonoff, David C. et al., “The Surveillance Error Grid”, Journal of Diabetes Science and Technology 2014, Vol. 8(4), 658-672.

Plot 4. Relative difference plot for the comparison study data points covering the measurement range of D-glucose in whole blood.

Mean and ±2 SD values are calculated from the displayed range of values. This (variant of Bland-Altman) plot of YSI 2900C vs YSI 2300 displays limits of the agreement interval (±2 SD) well within the published specifications. This level of relative difference bias of -1.3% in performance is very unlikely to cause any adverse impact in the medical decision relevant range.



Summary and Conclusion - Comparability

Summary

This study was done to gain a comparative performance description between the predicate instrument, YSI 2300 Biochemistry Analyzer and the YSI 2900C Biochemistry Analyzer. Data pairings were plotted, and the comparison described by a Deming weighted regression model, allowing for error on both axes. More than 99% of all the data pairs compared were within zone A of clinical risk for all bloodrelated matrices tested, for the whole range of glucose concentrations.

Conclusion

The device, the YSI 2900C Biochemistry Analyzer, performance was equivalent or better when compared to the predicate device, the YSI 2300 Biochemistry Analyzer for all four sample matrices tested. In conclusion, this study demonstrates the YSI 2900C Biochemistry Analyzer's ability to be an acceptable replacement for the YSI 2300 Biochemistry Analyzer as an In Vitro Diagnostic Device.

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