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**Brief communication (Original)**

# Variability of point-of-care testing blood glucometers versus the laboratory reference method in a tertiary teaching hospital

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***Background:*** Self-monitoring blood glucose (SMBG) has been established as a part of the point-of-care testing (POCT) in the management of patients diagnosed with diabetes mellitus. Various glucometers in the market have been used for this purpose but most are calibrated to whole blood. The recent recommendation by the International Federation of Clinical Chemistry (IFCC) is for glucose to be reported in plasma equivalent units which should correlate well with the clinical laboratory reference method. This is to minimize as much as possible the differences normally seen in the capillary whole blood glucose levels obtained during SMBG and routine plasma glucose levels reported by the laboratory.
***Objective:*** We evaluated the accuracy of four commercial blood glucose strips currently available in the local hospital setting against the laboratory reference method.
***Methods:*** We analyzed 145 whole blood samples collected into plain tubes from the walk-in patients in the hospital. A simultaneously whole blood sample was collected in sodium fluoride tubes and analyzed by the routine laboratory hexokinase method (RxL, Siemens). The four different types of glucometer strips used were AccuChek Performa, AccuChek Advantage, Abbott Optium and Johnson & Johnson Surestep.
***Results:*** The overall correlation coefficient for the four strips showed that the Accuchek Performa compared closest to the laboratory method which is R□=0.9761. This was followed by the Accuchek Advantage R□=0.9726. The Optium and Surestep systems showed R□=0.9376 and R□=0.9277 respectively. The coefficient variance (CV) for the Accuchek Performa is also <5% for both the control and sample precision. The ISO15197.2003 (E) acceptance criteria: percentage of individual results falling outside 0.8 mmol/L at glucose concentrations <4.1mmol/L and outside 20% of the reference result at glucose concentrations >4.1 mmol/L will not be higher than 5% showed that the compliance for Performa is 100% compared to the rest (for percentage of results within 95% compliance limit).
***Conclusion:*** The results showed that the Accuchek Performa system compared the closest to the laboratory method and complies to the ISO15197.2003 (E) with acceptable CV's.

***Keyword:*** Glucometers, glucose, POCT, variation

Diabetic patients, especially those who need insulin therapy, require careful monitoring to maintain control of blood glucose [1]. Self-monitoring of blood glucose (SMBG) as the point-of-care testing (POCT) enables patients to measure their own blood glucose concentration and modify their insulin dose based on this glucose value with the long-term aim of reducing and delaying complications. Portable meters complete with the test strips are available which permit a rapid and reasonably accurate measurements using the patient's capillary whole blood (finger prick). Traditionally, these strips have been calibrated against the standard laboratory reference methods (hexokinase) that actually utilize venous plasma or serum. However, whole blood glucose concentrations are approximately 10% to 15% lower than plasma or serum concentrations [2]. Therefore, the International Federation of Clinical Chemistry (IFCC) has recently recommended that glucose meters report the glucose concentration in plasma, irrespective of the sample type or technology [3]. This is to minimize as much as possible the differences seen in the measured glucose

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levels of capillary whole blood (in SMBG) and that of venous plasma or serum reported by the laboratory [2].

## Materials and methods

One hundred and forty five whole blood samples were collected into plain tubes from the walk-in patients attending the Diabetic Clinic, University Malaya Medical Centre, a 1000-bedded tertiary teaching hospital. This is a cross sectional study which had been approved by the Institutional Review Board of University Malaya Medical Centre. All possible effort was made to ensure that the ranges for hypo, normal and hyperglycemic samples were covered as sufficiently as possible. Upon phlebotomy, the whole blood was dropped immediately onto the four different glucometer test strips in duplicates. A second whole blood sample was collected simultaneously from each of the patients into a sodium fluoride tubes which was analyzed within 90 minutes by the reference laboratory glucose hexokinase method (RxL, Siemens). The calibration and control was done for each of the glucometers and the laboratory method daily before the tests commenced and strips were used according to the manufacturer instructions.

The Accu-Chek Performa® (Roche Diagnostics, Penzberg, Germany) is a new generation blood glucose strip that uses both AC and DC current to measure blood glucose levels in capillary blood. It utilises glucose dehydrogenase via a pyrroloquinoline mediator to measure glucose levels in the sample which are in turn reported based on internal strip specific calibration curves. This calibration curve has been constructed using a plasma (glucose hexokinase) reference method.

The Medisense Optium® *Point of Care* glucose strip (Abbott Diabetes, Alameda, CA) also utilizes glucose dehydrogenase via nicotine adenine dinucleotide as a mediator based on an internal strip-specific calibration curve. When the blood sample is applied to the test strip, the glucose in the blood reacts with the chemicals on the strip producing a small electrical current, this current is measured and results are displayed. According to the manufacturer's packaging insert this calibration curve has been established using a YSI glucose analyzer (YSI Inc) that uses whole blood for glucose measurements. However, the YSI whole blood glucose results are multiplied by a factor of 1.12 to provide plasma equivalent glucose values for calibration of the Medisense Optium ®*Point of Care* blood glucose strip. Results are obtained using a 2.5 μL sample within 20 seconds.

The Johnson and Johnson One-touch SureStep® test strips (LifeScan, CA) employs a dry reagent technology based on the glucose oxidase method which is specific for D-glucose. When a small drop of whole blood is applied to a SureStep® strip, glucose oxidase on the strip triggers the oxidation of glucose in the blood sample producing gluconic acid and hydrogen peroxide. Peroxidase on the test strip then causes the hydrogen peroxide to react with dyes to produce a blue colour in the presence of oxygen. This blue colour is visible through the confirmation dot on the back of the test strip. The colour intensity of this dot which is directly proportional to the level of glucose is measured and reported as a plasma-calibrated glucose result. The manufacturer's packaging insert stated that this strip method system was compared to that obtained from the YSI 2700 glucose analyzer to obtain the calibration curve.

The AccuCheck Advantage® (Roche Diagnostics, Penzberg, Germany) uses the glucose dehydrogenase enzyme method. In the presence of the coenzyme (PQQ), the glucose dehydrogenase enzyme on the test strip converts the glucose in the blood sample to glucunolactone. This reaction generates an electrical current that is interpreted by the meter as the glucose value. This method is referenced to and the strip calibrated against an automated hexokinase system which is traceable to an NIST standard.

A single lot number of each blood glucose strip was used for this study (AccuCheck Performa® strip Lot 14423901, Abbott Medisense Optium POC: strip Lot 53974, Johnson and Johnson One-touch SureStep® strip Lot 2788247011 and AccuCheck Advantage® II strip Lot 450026).

Data were analyzed by the Linear Regression, Bland & Altman and Error Grid descriptive analyses using the Analyze-it software.

## Results

Data from the performance evaluation of the four glucometer strips against the reference laboratory method are summarized in **Tables 1** and **2**.

Accucheck Performa compared the closest to the laboratory (hexokinase) method with a correlation coefficient ($R^2$)=0.9761, slope=0.9482 and intercept=0.4378 with a bias of 0.08 and the 95% confidence interval of -0.85 to 1.00. This confirms the

**Table 1.** Glucose strip results versus the hexokinase reference method.

| Glucometer system | Mean | 95% Confidence interval | % Difference |
|---|---|---|---|
| Performa® | 6.99 | 6.52-7.46 | -1.01 |
| Advantage® | 6.89 | 6.44-7.35 | 0.43 |
| Optium® | 8.05 | 7.54-8.57 | -16.3 |
| Surestep® | 7.62 | 7.05-8.18 | -10.1 |

**Table 2.** Summary of linear regression analysis

| Glucometer system | R□ | Intercept | Slope |
|---|---|---|---|
| Performa® | 0.9761 | 0.4378 | 0.9482 |
| Advantage® | 0.9726 | 0.4617 | 0.9364 |
| Optium® | 0.9376 | 1.3615 | 0.9662 |
| Surestep® | 0.9277 | 0.0211 | 1.0927 |

calibration coded by the manufacturer for the Accucheck Performa (slope=0.95 (95% CI 0.93-0.97), intercept= -0.04 (95% CI -0.16 to 0.07) with an adjusted R□ of 0.99.

The Accucheck Advantage was the second closest compared to the hexokinase method with the R□ of 0.9726 (95% CI -0.96 to 0.96) and zero bias. The Clarke Error Grid (**Figure 1**) showed that 99% of the measured values to be in zone A with only one value in zone B (>20% deviation from the reference; represents values that would lead to benign or no treatment error) but the Consensus Grid analyses showed 100% measured values to be in zone A.

Both the Abbott Medisense Optium (POC) and the Johnson and Johnson Surestep produced reasonable correlation coefficient when compared to the hexokinase method with R□ 0.9376 and 0.9277 respectively. The Abbott Medisense Optium showed a 95% CI of -0.31 to 2.58 with the largest bias of 1.13. The Clarke Error Grid (**Figure 2**) analysis also showed a relatively poor outcome with only 52% of measurements in zone A, 47% in zone B, and 1% in zone D (represent failure to detect and treat errors) while the Consensus Grid analysis produced a better picture with 73% of measurements in zone A and 27% in zone B.

## Discussion

The evaluation of glucose monitors is complex; therefore the glucose monitor evaluations must be carefully designed and executed in order to control protocol-specific bias and random patient interferences [7]. This study was done following as much as possible as per protocol and the steps did not deviate far from the proposed 14-step checklist for glucose monitor evaluation studies with associated references applicable to the international standard and consensus recommendations such as Standards for Reporting Diagnostic Accuracy (STARD), Clinical and Laboratory Standards Institute (CLSI) C30-A2 and EP9-A2, U.S Food and Drug Administration (USFDA), International Federation of Clinical Chemistry (IFCC) and International Standards Organization (ISO 15197) [4, 8, 9]. This is important to ensure that the blood glucometers in the market will have quality, consistency and accuracy in their reports of blood glucose values.

The Clarke Error Grid and Consensus Grid analyses (**Figure 3**) were able to demonstrate the reliability and accuracy of the Accucheck Performa with all 145 (100%) measured values to be in zone A (result leads to clinically correct treatment decisions either in hypoglycaemic or hyperglycaemic range). The Accucheck Performa also showed 100% ISO 15197.2003(E) compliance that confirms the clinical validity of the measured blood glucose values.

The Accucheck Advantage also showed excellent compliance to ISO 15197.2003(E) with 99.3% of results falling within compliance limits. This is a positive outcome when considering that Accucheck Advantage blood glucose measurement is whole blood calibrated and not plasma calibrated as per recommendation from IFCC.

**Table 3** displays the compliance to the ISO15197.2003(E) glucose monitoring international standard[4] where in the acceptance criteria states that the % of individual results falling outside 0.8 mmol/L at glucose concentrations <4.1 mmol/L and outside 20% of the reference result at glucose concentrations >4.1 mmol/L shall not be higher than 5%. The Abbott Medisense Optium was the least compliant to ISO 15197.2003(E) criteria based on this study with only 52.4% of blood glucose measurements falling in within the compliance limit.

The Johnson and Johnson SureStep had the 95% CI of -1.16 to 2.58 and the bias was 0.71. Its compliance to the ISO 15197.2003(E) was better than the Abbott Medisense Optium with 81.4% of measurements within the compliance limit. The Clarke Error Grid (**Figure 4**) analysis showed that the great majority (83%) of results were in zone A and 17% in zone B but the Consensus Grid analysis yielded a better result with 94% of measurements in zone A, 5% in zone B and 1% in zone C (represents values would lead to treatment decision opposite to that called for by the blood glucose levels).

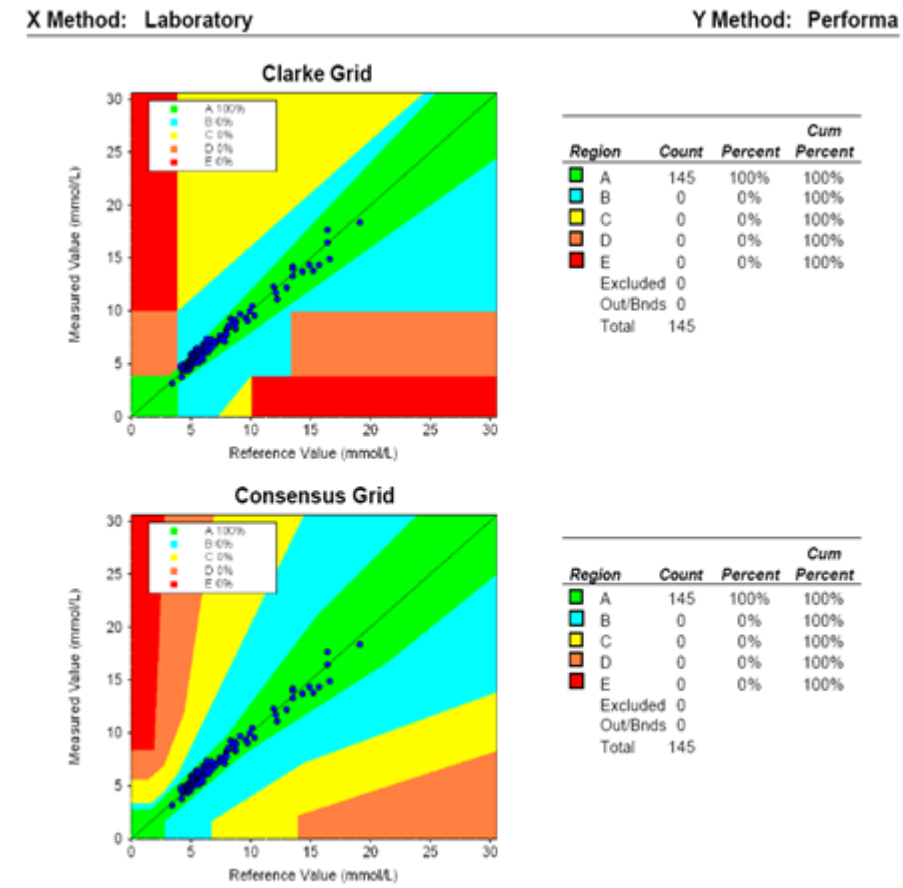



**Figure 1.** Clarke error grid and consensus grid analyses the accucheck advantage.

**Clarke error grid and consensus grid analyses (error grid analysis)**

This is an internationally recognized way [15] of evaluating the comparability of a blood glucose self-monitoring system with a laboratory reference. Evaluation is based on comparison of clinical consequences using the test strip method and the reference. This analysis partitions the total blood glucose range into zones, based on the effects of glucose variations on diabetes treatment:

Zone A: result leads to clinically correct treatment decisions either in hypoglycaemic or hyperglycaemic range

Zone B : >20% deviation from the reference; represents values that would lead to benign or no treatment error

Zone C: Represents values would lead to treatment decision opposite to that called for by the blood glucose levels

Zone D: Represent failure to detect and treat errors

Zone E: is a clinically more serious error zone, glucose meter generated values that failed to detect hypoglycaemia or hyperglycaemia. Values are opposite the reference values resulting in corresponding treatment decisions opposite to those needed.

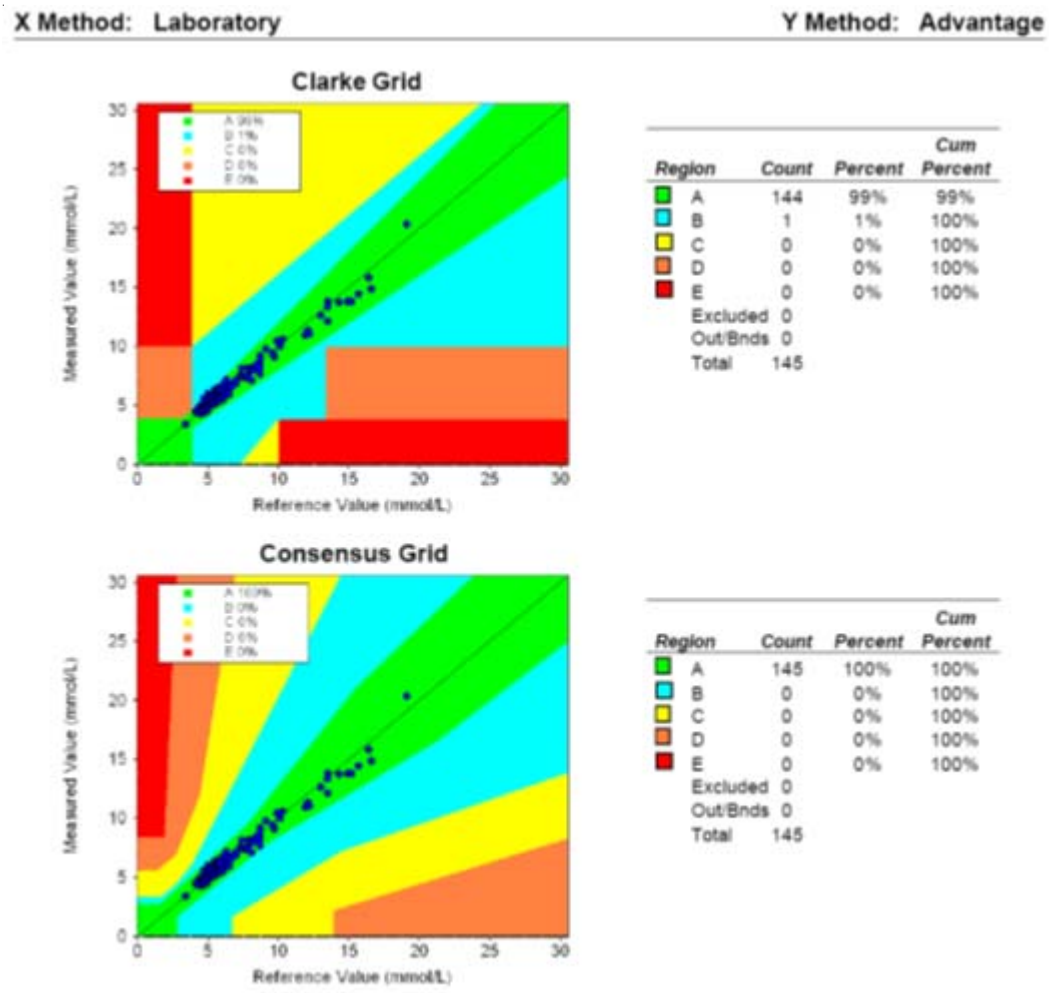



**Figure 2.** Clarke error grid and consensus grid analyses the abbott medisense optium**.**

However, the author would like to highlight a few limitations in this study. The number of extreme hypo- and hyperglycaemic values obtained were <5% of the total number of samples and this may affect the reliability of the values used to represent the functional sensitivity or minimum detection limit of each glucometer. Haematocrit was not measured in any of the samples which would have an influence in the acceptability of a few of the glucose results in the statistical analysis. Errors in measurement s made by these sensors on patients with increased haematocrit [10] e.g., polycythaemia may give falsely low glucose values generally and patients with anaemia or diabetic pregnant females with low haematocrit may produce falsely high blood glucose values [11].

## Conclusion

Critical care physicians and nurses in collaboration with point of care (POC) coordinators and clinical chemists should evaluate performance specifically as it relates to glucose intervals for tight glucose control protocols used in their own institutions [12, 13]. This is attributable to the fact that glucose meter systems may demonstrate characteristic accuracy patterns that may generate erroneous results and discrepant values. In addition, substantial and unpredictable differences in performance can affect patient care significantly. POC staff should scrutinize performance of these devices in order to minimize as much as possible the differences (normally seen) between capillary whole blood levels obtained during SMBG and routine plasma glucose levels reported by the clinical laboratory [14].

The authors have no conflict of interest to report.

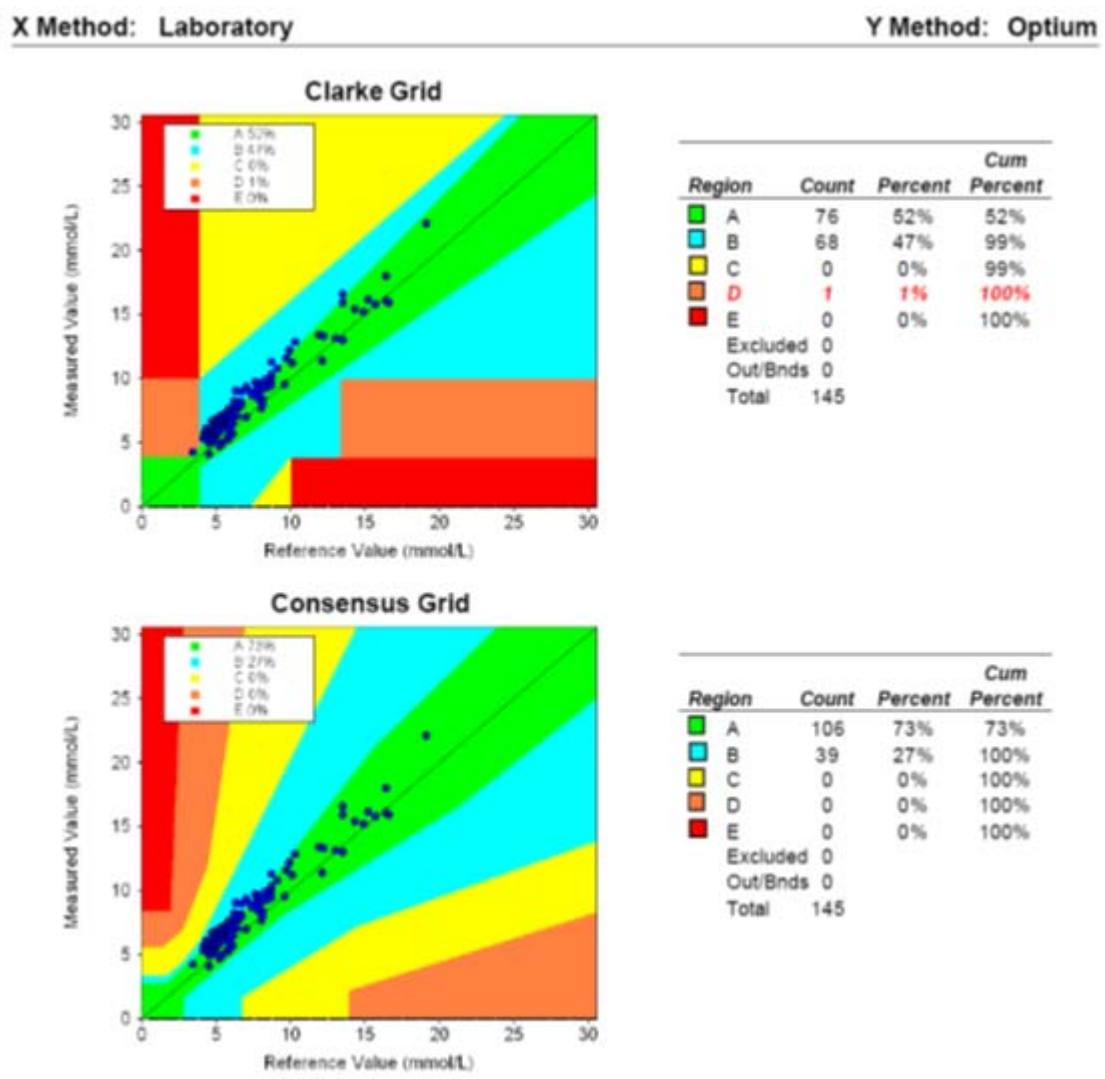



**Figure 3.** Clarke error grid and consensus grid analyses the accucheck performa.

**Table 3**. Compliance to ISO15197.2003 (E) glucose monitoring international standard.

| Glucometer System | % results within compliance limit (>95%) | % results outside acceptable limits (<5%) |
|---|---|---|
| Performa® | 100 | 0 |
| Advantage® | 99.3 | 0.7 |
| Optium® | 53.8 | 46.2 |
| Surestep® | 81.4 | 18.6 |

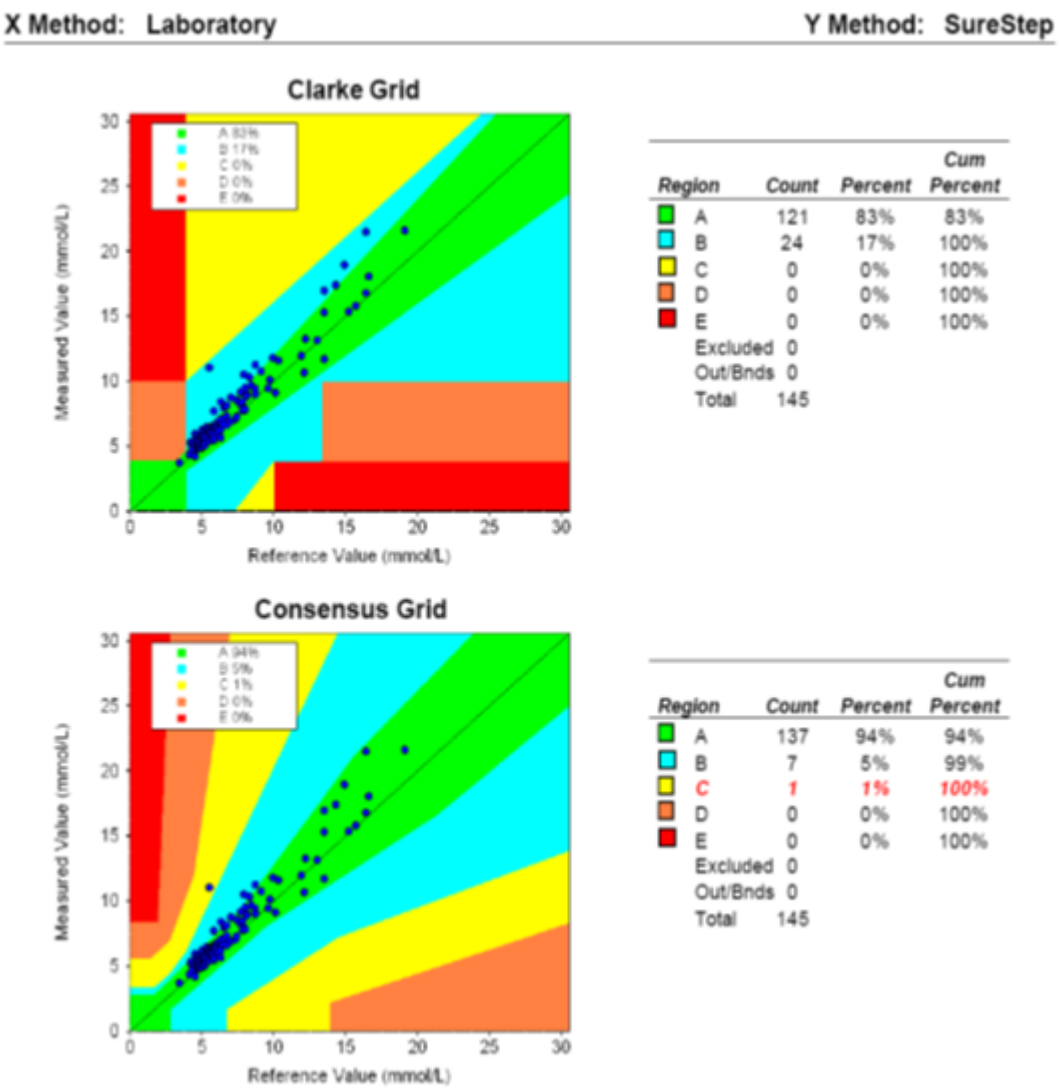



**Figure 4.** Clarke error grid and consensus grid analyses the Johnson and Johnson surestep.

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