EVALUATION OF THE PERFORMANCE OF THE TRUEBALANCE™ BLOOD GLUCOSE MONITORING SYSTEM USING THE *ISO 15197:2003 ACCURACY AND USER EVALUATION REQUIREMENTS*

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BACKGROUND:
The International Organization for Standardization (ISO) is well-respected worldwide as the largest developer and publisher of International Standards. In 2003, ISO established ISO 15197:2003. This standard specifies requirements for the accuracy of *in vitro* glucose monitoring systems that measure glucose concentrations in blood samples and procedures for the verification and the validation of performance by the intended users.

OBJECTIVE:
Demonstrate that the TRUEbalance™ Blood Glucose Monitoring System from Nipro Diagnostics, Inc. meets the standard for accuracy requirements established in ISO 15197:2003; and to demonstrate that users are able to achieve accurate results using the TRUEbalance™ System after minimal instructions for use and review of training materials.

METHODS:
A diverse study population of 100 patients over the age of 18 (19-79) currently being treated for, or recently diagnosed with, diabetes were recruited to participate in the study. Trained healthcare professionals were also recruited to participate.

ISO protocol requires two clinical evaluations — one by trained healthcare professionals and one by lay users — both using the TRUEbalance™ System. Healthcare professionals are required to obtain fingerstick blood samples from subjects for measurement using the TRUEbalance™ System and the standard laboratory reference instrument. Clinical accuracy is determined by comparing TRUEbalance™ results to laboratory results. The user performance evaluation consists of two tests, one comparing user results from two TRUEbalance™ Systems to the laboratory standard results, and one comparing two system user results to duplicate results obtained by a trained healthcare professional using the same blood sample.

Patients were asked to record their responses to five questions regarding clarity and understanding of the instructions, and how easy it was to perform a test using the TRUEbalance™ System based on a rating scale of 1 (poor) to 5 (excellent). Healthcare professionals also recorded an individual assessment of each subject's technique for each of five questions on the same rating scale. Acceptance criterion is an average score of 3.0 or greater for each question.

RESULTS:
The TRUEbalance™ System exceeds the minimum ISO standards for accuracy with 96.5% of results within the ISO defined limits. First-time users were able to obtain clinically accurate results when testing their blood glucose levels and healthcare professionals rated the TRUEbalance™ System favorably when observing users' compliance with the testing procedure.

CONCLUSIONS:
The TRUEbalance™ System meets ISO standards for accuracy and demonstrates accuracy, reliability and ease of use.

KEY WORDS:
TRUEbalance™, ISO, blood glucose monitoring system, accuracy, ease of use

OBJECTIVES

To demonstrate that the TRUEbalance™ Blood Glucose Monitoring System from Nipro Diagnostics meets the accuracy requirements set forth by *International Standardization Organization 15197:2003 In Vitro Diagnostic Test Systems — Requirements for Blood Glucose Monitoring Systems for Self-Testing in Managing Diabetes,* and to demonstrate that users are able to achieve accurate results using the TRUEbalance™ System after minimal instructions for use and training materials.

RESEARCH DESIGN

The study protocol was designed to comply with the requirements set forth in ISO 15197:2003, an international harmonized standard and FDA-recognized consensus standard. Trained healthcare professionals and 100 patients with diabetes participated in the study at one clinical research site. All subjects had a diagnosis of diabetes and were currently using a monitoring device. The ISO protocol requires two clinical evaluations, one with the healthcare professional using the device and one with the lay user (subject) using the device. Healthcare professionals trained on the device are required to obtain fingerstick blood samples from subjects for measurement using the TRUEbalance™ System and the standard laboratory reference instrument. Clinical accuracy is determined by comparing TRUEbalance™ results to laboratory results. The user performance evaluation consists of two tests, one comparing user results from two TRUEbalance™ Systems to the laboratory standard results, and one comparing two system user results to duplicate results obtained by a trained healthcare professional using the same blood sample. ISO 15197:2003 requires a user study to evaluate the device's instructions for use, and to evaluate each user's testing technique while under the observation of a healthcare professional. ISO 15197:2003 requires 95% of all results to be within +/- 15 mg/dL of the reference values for glucose levels less than 75 mg/dL and within +/- 20% of the reference values for glucose results greater than or equal to 75 mg/dL. If the data meets these criteria, then the device is considered to be clinically accurate and in compliance with ISO 15197:2003 requirements.

Table 1

ISO Category	Glucose Concentration Range	% Results Required for Clinical Evaluation
1	<50 mg/dL	5
2	50-80 mg/dL	15
3	81-120 mg/dL	20
4	121-200 mg/dL	30
5	201-300 mg/dL	15
6	301-400 mg/dL	10
7	>400 mg/dL	5

METHODOLOGY

The study population consisted of patients who are currently being treated for diabetes or have recently been diagnosed with type 1, type 2 or gestational diabetes. Age range of patients was 19-79 years with an average age of 57 years. Fifty-seven males and 43 females were recruited for the study. Ninety-six patients were Caucasian, three were Asian and one was African American. Selection criteria for a minimum of 100 patients was based mainly on diabetes patients who routinely monitor their blood glucose levels. Additional selection criteria consisted of age (greater than or equal to 18 years old), percent hematocrit (30–55%) and a required number (%) of glucose results within each of the ISO-defined glucose concentration ranges (Table 1). Patients exhibiting hematocrit levels less than 30% or greater than 55%, or patients who had documented medication interferences, were excluded from the study. Each potential study participant was screened by performing TRUEbalance™ tests using fingertip samples. If TRUEbalance™ results fell within one of the defined glucose concentration ranges, and all other inclusion criteria were met, then the patient was accepted to participate in the study. Once the required number of results was reached in each glucose concentration range, no more results could be added.

DATA COLLECTION

Healthcare Professional Testing

All testing was performed at the clinical site. Prior to patient testing each day, quality control tests were performed on TRUEbalance™ Meters and TRUEbalance™ Strips per manufacturer's instructions for use. Healthcare professionals collected all patient blood samples used for testing. The first test sequence included five capillary fingerstick blood samples, one sample for measurement of hematocrit, two samples for measurement using the laboratory reference instrument, and two samples for measurement using two TRUEbalance™ Meters. All sampling was completed within ten minutes.

User Performance Evaluation

For the second sequence of testing, both patients and healthcare professionals performed blood sampling and testing. Patients were provided TRUEbalance™ Instructions For Use for review and asked to obtain duplicate fingerstick capillary blood to use for testing using two different TRUEbalance™ Systems. The healthcare professional or other study investigator was not allowed to intervene or answer questions by the patients during testing. Once patient testing was completed, a healthcare professional obtained duplicate fingerstick samples from the subjects for testing using the same two TRUEbalance™ Systems. The healthcare professional also collected duplicate blood samples for the laboratory reference instrument and one sample to measure hematocrit. All testing was completed within ten minutes. Every effort was made to obtain all samples from the same fingerstick.

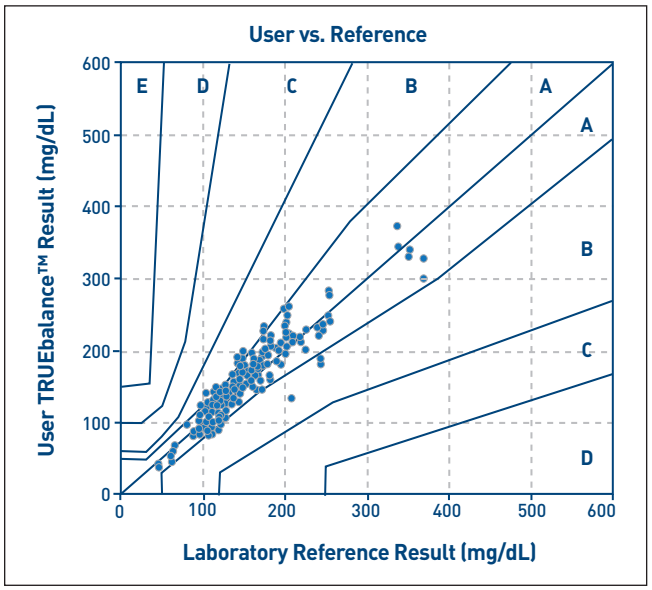
An evaluation by 50 patients was performed to assess the clarity of the TRUEbalance™ Instructions For Use and the users' abilities to follow the instructions for use during the testing procedure. After reviewing the TRUEbalance™ Instructions For Use, patients were asked to record their responses to five questions regarding clarity and understanding of the instructions, and how easy it was to perform a test using the TRUEbalance™ System.

Ratings were scaled from 1 (poor) to 5 (excellent) for each of five questions. Healthcare professionals observed patients' techniques and compliance to the instructions for use while performing tests using the TRUEbalance™ System. Healthcare professionals recorded an individual assessment of each subject's technique based on a rating scale of 1 (poor) to 5 (excellent).

DATA ANALYSIS

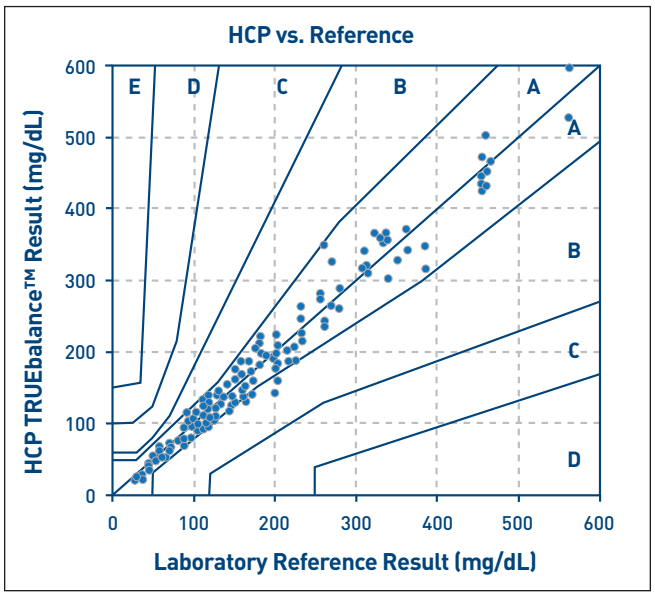
As outlined in ISO 15197:2003, data analysis must be performed and reported to a statistically justifiable analysis. To determine whether the system meets ISO 15197:2003 acceptance criteria for accuracy, ISO requires using a bias plot to show system accuracy. The bias is measured at each glucose concentration interval and results are represented below the 75 mg/dL limit and greater than or equal to 75 mg/dL. ISO defines acceptable accuracy as 95% of all glucose results, both less than 75 mg/dL and greater than or equal to 75 mg/dL, must fall within the ISO limits as defined in Table 2. Parkes et al. developed an error grid to analyze the clinical significance of the bias between the blood glucose monitor results and the lab results. For this analysis, an error grid was used to assign data points into one of the five Zones A-E. This analysis was repeated using the data for the HCP (Healthcare Professional) TRUEbalance™ results compared to lab results, the user results compared to the lab results, and the user results compared to the HCP results. For all three comparisons, 100% of data points fell into Zones A and B, which is defined as clinically acceptable and any observed difference in results would not lead to a treatment decision that may put a subject at risk. As the bias or difference increases between the results (Zones C, D and E), there is greater risk in terms of under-treating or over-treating the patient based on the glucose result. The graphs on page 4 provide the error grid analysis of TRUEbalance™ user results (Figure 1) and healthcare professional results (Figure 2) compared to laboratory reference, as well as TRUEbalance™ user results compared to healthcare professional results using the same systems (Figure 3).

Figure 1: TRUEbalance™ System user results compared to laboratory reference results using Parkes Error Grid.



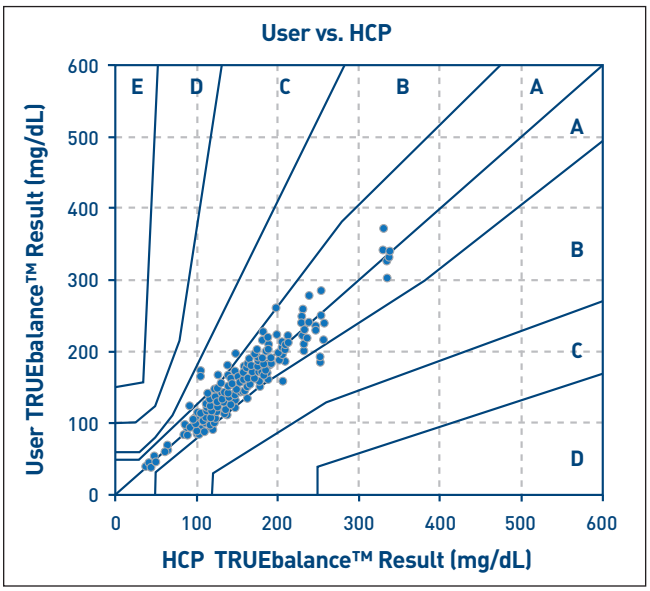
100% of results were in Zones A and B

Figure 2: TRUEbalance™ healthcare professional results compared to the laboratory reference results using Parkes Error Grid.



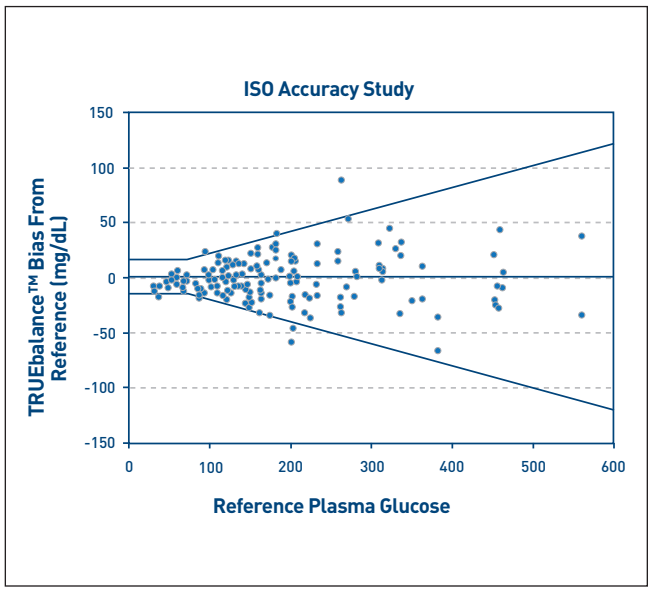
100% of results were in Zones A and B

Figure 3: TRUEbalance™ user results compared to healthcare professional results using the TRUEbalance™ System.



100% of results were in Zones A and B

Figure 4: Bias plot for the TRUEbalance™ System results compared to the laboratory results.



TRUEbalance™ System meets the ISO criteria for accuracy with 96.5% of results within the limits

Table 2: ISO defined limits

Glucose Concentration	ISO Limits	Criteria for Accuracy
Less than 75 mg/dL	+/- 15 mg/dL	95% of all results must be within ISO limits
Greater than or equal to 75 mg/dL	+/- 20%	

USER EVALUATION

Users were asked to evaluate TRUEbalance™ Instructions For Use and ease-of-use of the system. Ratings were based on a scale of 1 (poor) to 5 (excellent). The acceptance criterion was a score of 3.0 or greater. An average of ratings for each question is outlined in Table 3.

To evaluate users' compliance to the instructions for use, healthcare professionals were asked to observe each user during testing with the TRUEbalance™ System and to complete a short questionnaire. Ratings were based on a scale of 1 (poor) to 5 (excellent). The acceptance criterion was an average score of 3.0 or greater for each question. The questions and corresponding ratings are provided in Table 4.

Table 3

Questions	Average User Rating
Were the instructions easy to understand?	4.3
Did the instructions adequately describe how to apply the blood?	4.6
Were the instructions clear on how to read the results?	4.7
Was the display easy to read?	4.9
Was the system easy to use?	4.6

Table 4

Questions for HCP Evaluation of Patient During Testing With TRUEbalance™ System	Average User Rating
Did patient insert strip correctly?	4.3
Did patient apply blood correctly?	4.4
Did patient read result correctly?	4.9
Did patient follow the written instructions?	4.5

CONCLUSION

The TRUEbalance™ Blood Glucose Monitoring System from Home Diagnostics meets the accuracy requirements of International Standardization Organization 15197:2003. Both healthcare professionals and first-time users of the TRUEbalance™ System obtained clinically accurate results when compared to the laboratory standard.

Using the Parkes Error Grid to determine the clinical significance between the differences in the TRUEbalance™ results and the laboratory standard showed all results obtained by users and professionals fell within the clinically accurate Zones A and B.

Without receiving hands-on instruction from professionals on use of the TRUEbalance™ System, first-time users were able to obtain clinically accurate results when testing their blood glucose levels. Users rated the system as easy to use and understand the instruction. Healthcare professionals rated the TRUEbalance™ System favorably when observing users' compliance with the testing procedure. The results of this study demonstrate that the TRUEbalance™ System is accurate, reliable, easy to use, and can be recommended for people with all types of diabetes.

FOR ADDITIONAL INFORMATION OR QUESTIONS, ADDRESS WRITTEN REQUESTS TO:

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Reference

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