WaveSense™ White Paper:
Performance of the WaveSense KeyNote™ Blood Glucose Monitoring System Across 23 Lots of Test Strips

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WaveSense™

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Abstract

A few well-known variables that impact system accuracy include sample characteristics such as hematocrit, testing environment such as ambient temperature and humidity and manufacturing errors such as lot-to lot variability in reagent strips. Pharmacologic agents are also known to interfere with the accuracy of glucose measurements[1]. Many of these variations are "corrected" by WaveSense™; thus the KeyNote™ system powered by WaveSense has the ability to provide results that are accurate.

Study Method

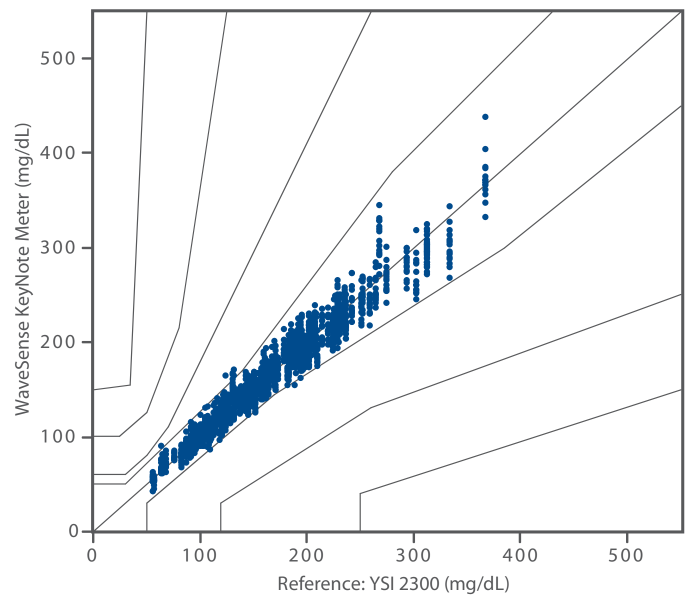
For this study, a total of 23 different lots of WaveSense KeyNote test strips were evaluated at three different times at two distinct clinical sites. Each study was conducted over two days. Site 1 (Internal Medicine and Endocrinology, Inc, Worcester, MA, USA) evaluated 8 unique lots with 50 patients and 7 unique lots with 52 patients. Site 2 (Diabetes, Endocrine & Nutrition Center, Hampton, NH, USA) evaluated 8 unique lots with 48 patients (A total of 4 participant results were excluded due to insufficient plasma to obtain an YSI reading and 7 individual readings were excluded because of meter error). A whole blood capillary sample was obtained by finger stick from each participant. Each whole blood capillary sample was then introduced into two strips from each lot and the glucose reading recorded. Whole blood was then collected into capillary tubes, which were centrifuged and the supernatant plasma extracted. The plasma glucose concentration was then measured using an YSI 2300 STAT Plus Glucose Analyzer.

Accuracy Results

The individual results from the WaveSense KeyNote meter were plotted on the Parkes Error Grid[2] against the YSI (reference) value. The Parkes Error Grid is divided into 5 zones. Each Zone represents the significance of the error in a glucose reading as it relates to making a clinical decision based on the glucose reading.

Zone A: No effect on clinical outcome.
Zone B: Altered clinical action with 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 risk.
Zone E: Altered clinical action could have dangerous consequences.

The data presented in the Parkes Error Grid below and Table 1 indicates that 99.5% of the glucose readings obtained during the study are within the clinically accurate Zone A.



n=2289

Table 1

Zone A	Zone B	Zone C	Zone D	Zone E
2277/2289 (99.5%)	12/2289 (0.5%)	0/2289 (0%)	0/2289 (0%)	0/2289 (0%)

Table 2

For reference concentrations <75 mg/dL		
Within ±5mg/dL	**Within ±10mg/dL**	**Within ±15mg/dL**
49/74 (66.2%)	65/74 (87.8%)	71/74 (95.9%)

For reference concentrations ≥75 mg/dL			
Within ±5%	**Within ±10%**	**Within ±15%**	**Within ±20%**
1162/2215 (52.5%)	1881/2215 (84.9%)	2136/2215 (96.4%)	2197/2215 (99.2%)

Measured Variables

Hematocrit: Study participants had a hematocrit range from 25.1-54.4%. Hematocrit is a measure of the percentage of red blood cells to the total blood volume and can have a physiological range of approximately 35-50% and is typically observed to be higher in men than women and individuals who reside at higher altitudes. Clinically acceptable variations in hematocrit, unfortunately, impact the performance of SMBG systems and introduce error[3]. The most important reason is that a higher hematocrit results in closer physical approximation of the red blood cells in the expressed sample and retards or impedes the mobility of the analyte (glucose and/or mediator (reagent). Thus a higher hematocrit results in a lowered measured blood glucose reading.

A reliable measurement of glucose concentration without undue influence from hematocrit is desirable. The data above shows the ability of WaveSense technology to correct for hematocrit and provide accurate readings across a broad range.

Temperature and humidity: Each of the 3 studies was conducted over a span of 2 days in an indoor clinical environment. The ambient temperature varied from a mimimum of 20.7 °C to 26.0 °C during this testing period. At the same time, the humidity varied from <15% to 37%. These environmental parameters are known to influence SMBG measurements[4]. Often, people test themselves in dynamically changing climatic conditions in contrast to the controlled clinical environments depicted in clinical studies. Therefore, it would be ideal to have a meter that corrects for these environmental variations without undermining the accuracy.

A. Manufacturing Variation

Sixteen unique WaveSense KeyNote meters and 23 different reagent strip lots were used to measure the capillary blood expressed. Inherent manufacturing variations manifest themselves in the reagent strips used to measure glucose. Minor differences in test area geometry, reagent deposition and drying can impact the final measurement significantly. A greater scrutiny and quality control process can minimize these manufacturing variations but it is nearly impossible to eliminate them.

B. Study Site Characteristics

A total of 154 adult patients participated in this study. The studies were conducted in 2 different clinical sites at 3 different points in time during March-May 2007. Each study was conducted over 2 days. Trained healthcare professionals conducted the study, an approved IRB protocol was followed, the trial was conducted under Principal Investigator (PI) oversight and the PI verified the accuracy of the data.

C. Demographic Diversity

Patient demographic was diverse. Both male (n=73) and female patients (n=81) with a wide age range (21-79 years) participated in the study. All these patients had been diagnosed to have either Type 1 (n=46) or Type 2 (n=108) diabetes. Patients learned about their diagnosis as recently as 8 months prior to the study while others had been managing their health for a long time (56 years).

Conclusion

The performance of these reagent strip lots exceeds the guidelines of the ISO 15197. As is evident, the WaveSense KeyNote system provides highly accurate results despite the effects of a diverse patient demographic, a wide range of hematocrit, differences in 23 lots of reagent test strips and environmental influences of temperature and humidity.

About WaveSense

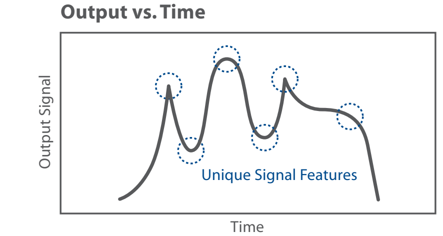
The WaveSense KeyNote Blood Glucose Monitoring (BGM) system, manufactured by AgaMatrix, Inc., measures glucose concentration in a sample of fresh capillary whole blood. WaveSense uses Dynamic Electrochemistry™ coupled with specific signal processing algorithms to correct for a number of errors that are common in self-monitoring blood glucose (SMBG) systems, resulting in more accurate and repeatable measurements. This white paper presents the clinical data to highlight the system accuracy (analytical and clinical accuracy) of the WaveSense KeyNote system across 23 different strip lots and highlights the corrective performance of the WaveSense KeyNote system.

All SMBG systems in major markets (US/Europe) must meet the International Organization for Standardization (ISO) 15197:2003[5], specifying that 95% of glucose results must be within ± 20% of a reference standard (for results at or above 75mg/dL) and within ± 15mg/dL (for results below 75mg/dL). WaveSense™ technology enables the KeyNote meter to exceed this standard across 23 different strip lots with multiple factors that have been known to impact accuracy of SMBG systems.

WaveSense KeyNote uses: WaveSense *Dynamic Electrochemistry*

A time-varying input signal from the KeyNote meter induces an output signal that is much more information rich, which can then be exploited by sophisticated digital signal processing algorithms to give an accurate glucose reading.

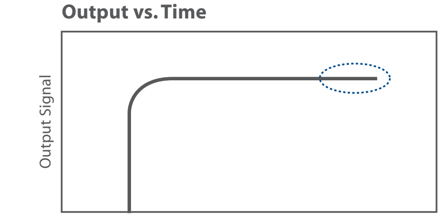
Output vs. Time



Many other leading SMBG systems use: *Static Electrochemistry*

A fixed input signal (such as an applied voltage) from the blood glucose meter results in an output signal that correlates to the glucose concentration in the sample.

Output vs. Time



[1] Tang, ZP, Du XG, Louie R.F., Kost G.J. 51st Annual AACC conference, July 25-29, 1999, New Orleans, Louisiana
[2] Parkes, J.L., Pardo S., Slatin S.L., Ginsberg G.H. A new consensus Error Grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. Diabetes Care; 23:1143-1148, 2000.
[3] Tang, Z. L. (2000). Effects of Different Hematocrit Levels on Glucose Measurements with Hand Held Glucose Meters. Arch. Pathol. Lab Med. 1135-1140.
[4] Michael J. Haller, Johnathan J. Shuster, Desmond Schatz, Richard J. Melker. Diabetes Technology & Therapeutics. February 1, 2007, 9(1): 1-9
[5] ISO 15197:2003. In vitro diagnostic test systems —Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.