White Paper, Evaluation of WaveSense JAZZ™ Blood Glucose Monitoring System Analytical Performance to EN ISO 15197:2015 Standard

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Executive Summary

In light of the introduction of the updated EN ISO 15197:2015, the analytical performance of the WaveSense JAZZ™ blood glucose monitoring system was evaluated against the updated performance requirements published in the standard. The WaveSense JAZZ™ blood glucose monitoring system meets all the analytical performance requirements of the EN ISO 15197:2015 standard.

Changes introduced in EN ISO 15197:2015

Updated requirements for blood glucose monitoring systems have been published in EN ISO 15197:2015 standard (1). The new standard has some updated requirements and a few new requirements. Significant changes to the standard are summarized below.

Precision

The requirements in this section were updated to include testing on three lots of test strips.

System Accuracy

The blood glucose monitoring system shall meet both of the following minimum criteria for acceptable system accuracy

A. 95% of the measured glucose values shall fall within either ± 0.83 mmol/l (±15 mg/dl) of the average measured values of the reference measurement at glucose concentrations < 5.55 mmol/l (<100 mg/dl) or within ± 15% at glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl).
B. 99% of individual glucose measured values shall fall within zones A and B of the Consensus Error Grid (CEG) for type 1 diabetes.

Criterion A shall be applied to each reagent lot individually. The measured values from each lot shall be analyzed and reported separately.
Criterion B shall be applied to the three reagent lots taken together.

Haematocrit

This is a new requirement in EN ISO 15197:2015 standard.
The packed cell volume effects shall be described in the instructions for use if they meet either of the following performance criteria.

- For glucose concentrations < 5.55 mmol/l (< 100 mg/dl), the difference between the average measured value at each haematocrit level and the average measured value at the nominal haematocrit exceeds 0.55 mmol/l (10 mg/dl).
- For glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl), the difference between the average measure value at each haematocrit level and the average measured value at the nominal haematocrit exceeds 10%.

Chemical Interference

This is a new requirement in EN ISO 15197:2015 standard.
The interference effects shall be described in the instructions for use if they meet either of the following performance criteria.

- For glucose concentrations < 5.55 mmol/l (< 100 mg/dl), the average difference between the test sample and the control sample exceeds 0.55 mmol/l (10 mg/dl).
- For glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl), the average difference between the test sample and the control sample exceeds 10%.

User Performance Evaluation

The requirements in this section were updated to include testing one lot of test strips.

Precision

The precision of the WaveSense JAZZ™ blood glucose monitoring system (BGMS) was evaluated according to EN ISO 15197:2015 standard, section 6.2.

Repeatability (Within-Run Precision)

Method

Repeatability was evaluated according to EN ISO 15197:2015, section 6.2.3, at five glucose concentrations across the system measuring range. Thirty six blood glucose meters were tested with thirty six individual vials of test strips, twelve vials from each of three lots. Ten replicate measurements were made for each meter for each of the five assigned glucose levels of blood.

Results

Grand Mean, mmol/L (mg/dl)	Pooled Standard Deviation, mmol/L (mg/dl)	Pooled Coefficient of Variation
1.98 (35.7)	0.13 (2.3)	N/A
4.88 (88.0)	0.18 (3.2)	N/A
7.04 (126.9)	0.20 (3.6)	2.8%
12.40 (223.5)	0.32 (5.8)	2.6%
21.39 (385.4)	0.62 (11.2)	2.9%

Conclusion

The WaveSense JAZZ™ blood glucose monitoring system exhibits excellent repeatability across the system measurement range.

Intermediate Precision (Day-to-Day Precision)

Method

Intermediate precision was evaluated according to EN ISO 15197:2015 section 6.2.4. Three lots of strips were tested at three control solution levels, using three operators. Each control solution level was measured once per day on each of 12 meters. This testing was performed over 10 days.

Results

Grand Mean, mmol/l (mg/dl)	Pooled Standard Deviation, mmol/l (mg/dl)	Pooled Coefficient of Variation (%)
3.05 (54.9)	0.11 (2.0)	N/A
7.16 (129.0)	0.24 (4.3)	3.3
17.62 (317.6)	0.72 (13.0)	4.1

Conclusion

The WaveSense JAZZ™ blood glucose monitoring system exhibits excellent intermediate precision across the system measurement range.

System Accuracy

System accuracy of the WaveSense JAZZ™ BGMS was evaluated according to EN ISO 15197:2015, section 6.3.

Requirement

The minimum acceptable accuracy performance criteria are specified in EN ISO 15197:2015, section 6.3.3.

The blood-glucose monitoring system shall meet both of the following minimum criteria for acceptable system accuracy:

A. 95% of the measured glucose values shall fall within either ± 0.83 mmol/l (± 15 mg/dl) of the average measured values of the reference measurement at glucose concentrations < 5.55 mmol/l (< 100 mg/dl) or within ± 15% at glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl).

B. 99% of individual glucose measured values shall fall within zones A and B of the Consensus Error Grid (CEG) for type 1 diabetes.

Criterion A shall be applied to each reagent lot individually. The measured values from each lot shall be analyzed and reported separately.

Criterion B shall be applied to the 3 reagent lots taken together. All measured values from the 3 lots shall be combined before analysis and reporting.

Method

System accuracy was evaluated using fresh blood samples from 100 study participants, and was conducted in conditions reflecting actual conditions of use. Three lots of test strips were used in the study. The blood glucose concentrations of the samples were targeted to be distributed as in the below table, per EN ISO 15197:2015.

Bin #	Percentage of samples (%)	Glucose Concentration mmol/l (mg/dl)
1	5	≤ 2.77(≤ 50)
2	15	> 2.77 to 4.44 (> 50 – 80)
3	20	> 4.44 to 6.66 (> 80 – 120)
4	30	> 6.66 to 11.10 (> 120 – 200)
5	15	> 11.10 to 16.65 (> 200 – 300)
6	10	> 16.65 to 22.20 (> 300 – 400)
7	5	> 22.20 (> 400)

The reference plasma glucose concentrations of the samples were determined by Yellow Springs Instruments (YSI) 2300 STAT Plus before and after testing with the BGMS. According to EN ISO 15197:2015 section 6.3.5, if the study population does not provide sufficient samples in the lowest and highest glucose concentration categories shown in the table above, these may be supplemented with modified blood samples in which the glucose concentration has been raised or lowered. In this study, modified samples were used to supplement bin 1 (5 samples), bin 2 (4 samples) and bin 7 (4 samples).

Results

Accuracy Criterion A

The difference between each individual BGM reading and its corresponding YSI 2300 STAT Plus plasma glucose reference concentration for all the three test strip lots is shown in the system accuracy difference plot, Figure 1. All three lots of test strips met the system accuracy acceptance criterion A. Overall, greater than 99% of readings met accuracy criterion A.

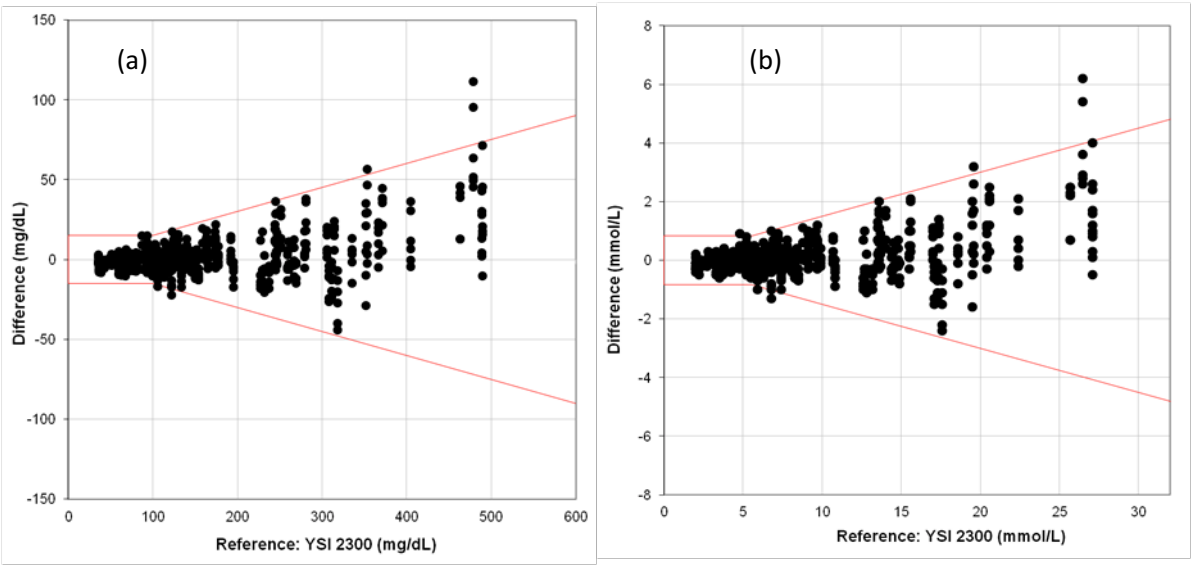

Figure 1: System accuracy plot for BGMS glucose vs. YSI 2300 plasma glucose concentration (a) mg/dl units and (b) mmol/l units. Data shown is from three test strip lots. Area inside the solid lines represents minimum acceptable accuracy from EN ISO 15197:2015.

Table 1: Summary of system accuracy results for each lot at all glucose concentrations

Lot	System Accuracy Results for glucose concentrations		
	< 5.55 mmol/l (< 100 mg/dl), Within ± 0.83 mmol/l (± 15 mg/dl)	≥ 5.55 mmol/l (≥ 100 mg/dl), Within ±15%	All glucose concentrations
KF06WE46I	58/58 (100%)	140/142 (98.6%)	198/200 (99.0%)
KJ21WD78G	58/58 (100%)	141/142 (99.3%)	199/200 (99.5%)
KJ29WE16I	57/58 (98.3%)	140/142 (98.6%)	197/200 (98.5%)
Combined	173/174 (99.4%)	421/426 (98.8%)	594/600 (99.0%)

Table 2: Overall system accuracy results

System accuracy results for glucose concentrations < 5.55 mmol/l (< 100 mg/dl)		
Within ± 0.28 mmol/l (± 5 mg/dl)	Within ± 0.56 mmol/l (± 10 mg/dl)	Within ± 0.83 mmol/l (± 15 mg/dl)
120/174 (69.0%)	170/174 (97.7%)	173/174 (99.4%)
System accuracy results for glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl)		
Within ±5%	**Within ±10%**	**Within ±15%**
256/426 (60.1%)	387/426 (90.9%)	421/426 (98.8%)
System accuracy results for all the glucose concentrations, Within ± 0.83 mmol/l (± 15 mg/dl) and ±15%		
594/600 (99.0%)		

Accuracy Criterion B

The consensus error grid in Figure 2, shows that 600/600 (100%) values fall within zone A, defined as "no effect on clinical action" (2).

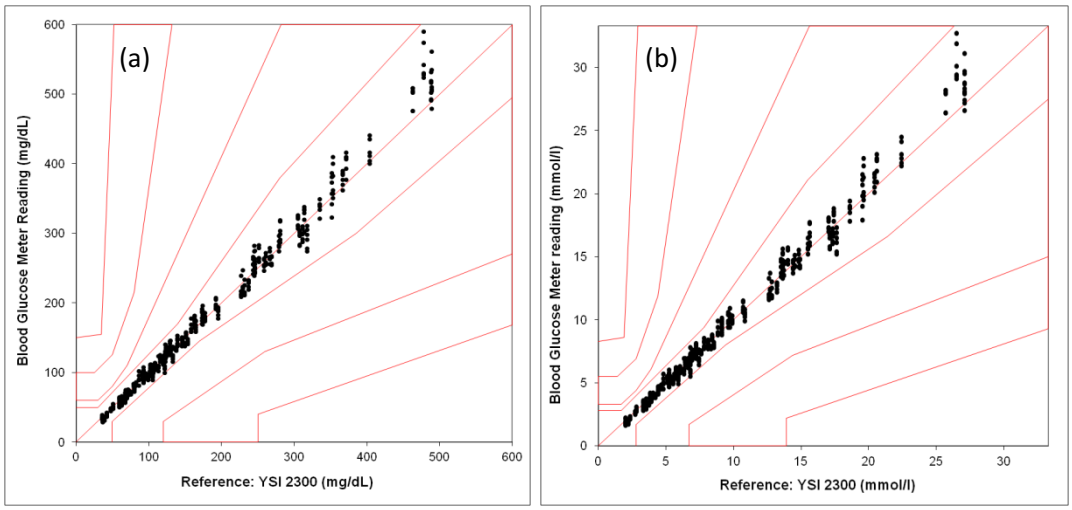

Figure 2: Plot of BGMS glucose concentrations vs. YSI 2300 plasma glucose concentrations. (a) mg/dl units and (b) mmol/l units

Conclusion

The WaveSense JAZZ™ blood glucose monitoring system meets and exceeds the minimum acceptable system accuracy criteria specified in EN ISO 15197:2015.

Haematocrit

The effect of sample haematocrit (packed cell volume) on the accuracy of the WaveSense JAZZ™ BGMS was evaluated according to EN ISO 15197:2015, section 6.4.3.

Requirement

Acceptance criteria for haematocrit evaluation are specified in EN ISO 15197:2015, section 6.4.3.2 as below:

The packed cell volume effects shall be described in the instructions for use if they meet either of the following performance criteria.

- For glucose concentrations < 5.55 mmol/l (<100 mg/dl), the difference between the average measure value at each haematocrit level and the average measured value at the nominal haematocrit exceeds 0.55 mmol/l (10 mg/dl).
- For glucose concentrations ≥ 5.55 mmol/l (≥100 mg/dl), the difference between the average measure value at each haematocrit level and the average measured value at the nominal haematocrit exceeds 10%.

Method

The effect of sample haematocrit was evaluated according to EN ISO 15197:2015, using whole blood samples with haematocrit levels between 20-60% and glucose concentrations across the system measurement range. Testing was performed at each combination of haematocrit (nine levels, at 5% increments) and three glucose levels (2.2 mmol/l, 6.9 mmol/l, 19.4 mmol/l), resulting in a total of 27 haematocrit and glucose combinations. Three lots of test strips were evaluated using ten blood glucose meters. Each blood sample was measured on ten test strips per lot.

Results

Mean bias in meter results at each haematocrit and nominal haematocrit (40%) at each glucose and haematocrit level is shown in the graph below (Figure 3). Across all strip lots, 99.5% of the meter readings fell within ± 0.83 mmol/l (±15 mg/dl) or ± 15% of the YSI reference glucose measurement.

Acceptance Criteria	Result (across 3 strip lots)
For glucose concentrations < 5.55 mmol/l (< 100 mg/dl), the mean bias in meter results between each haematocrit and nominal haematocrit (40%) will not exceed ± 0.55 mmol/l (± 10 mg/dl) .	Less than ± 0.22 mmol/l (Less than ± 4 mg/dl)
For glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl), the mean bias in meter results between each haematocrit and the nominal haematocrit (40%) will not exceed ± 10%.	Less than ± 7.7%

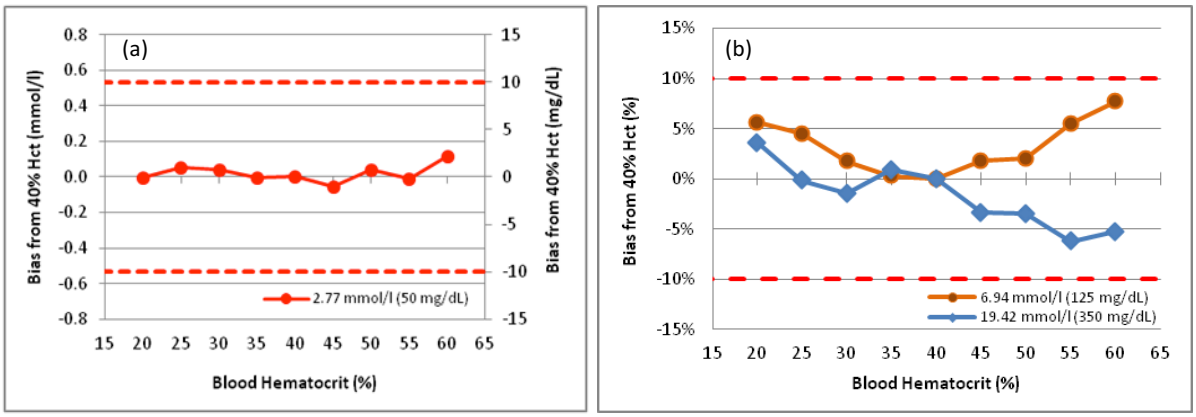

Figure 3: Mean Bias for Glucose Level 1 (a) and Levels 2 & 3 (b)

Conclusion

The WaveSense JAZZ™ blood glucose monitoring system meets and exceeds the acceptance criteria for haematocrit (packed cell volume) bias specified in EN ISO 15197:2015 for the range 20-60%.

Chemical Interference

The effect of chemical interferents on the accuracy of the WaveSense JAZZ™ BGMS was evaluated according to EN ISO 15197:2015, Section 6.4.4.

Requirement

Acceptance criteria for interference evaluation are specified in EN ISO 15197:2015, section 6.4.4.2 as below:

The interference effects shall be described in the instructions for use if they meet either of the following performance criteria.

- For glucose concentrations < 5.55 mmol/l (< 100 mg/dl), the average difference between the test sample and the control sample exceeds 0.55 mmol/l (10 mg/dl).
- For glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl), the average difference between the test sample and the control sample exceeds 10%.

Method

The effect of potential chemical interferents was established by evaluating bias in glucose readings between low/none and high interferent concentrations at three different glucose levels. The high interferent concentration was chosen to be representative of pathological (endogenous)/toxic (exogenous) concentrations, and was based on CLSI EP7-A2 recommendation where applicable (3). A total of 31 potential chemical interferents were assessed, using whole blood samples. Ten replicates were collected per test condition, using ten blood glucose meters. Testing was performed with three lots of test strips. Data were collected, organized, summarized and tabulated according to CLSI EP7-A2 requirements.

Results

The performance of the BGMS with respect to the chemical interference requirements is summarized in the table below. All potential interferents except ascorbic acid were tested to pathological (endogenous)/toxic (exogenous) concentrations and found to show no significant bias (i.e., <10% bias or ≤ ± 0.55 mmol/l (± 10 mg/dl)). Ascorbic acid did not show any significant bias up to 0.17 mmol/l.

Chemical	Highest Concentration without significant effect on results
Acetaminophen	20 mg/dL (1.32 mmol/L)
Ascorbic acid	3 mg/dL (0.17 mmol/L)
Bilirubin, conjugated	29 mg/dL (0.34 mmol/L)
Bilirubin, Free	20 mg/dL (0.34 mmol/L)
Caffeine	6 mg/dL (0.31 mmol/L)
Ceftriaxone	97 mg/dL (1.46 mmol/L)
Cholesterol	600 mg/dL (15.50 mmol/L)
Creatinine	5 mg/dL (0.44 mmol/L)
Dopamine	0.09 mg/dL (5.9 μmol/L)
EDTA	0.1 mg/dL (3.4 μmol/L)
Fructose	18 mg/dL (1.00 mmol/L)

Galactose	120 mg/dL (6.72 mmol/L)
Gentisic acid	1.8 mg/dL (0.12 mmol/L)
Glutathione	92 mg/dL (3 mmol/L)
Hemoglobin	200 mg/dL (31 μmol/L)
Heparin	1.9 mg/dL (3 kU/L)
Ibuprofen	50 mg/dL (2.43 mmol/L)
Icodextrin	1094 mg/dL (686 μmol/L)
Lactose	10 mg/dL (0.29 mmol/L)
L-DOPA	4 mg/dL (0.20 mmol/L)
Maltose	278 mg/dL (8.1 mmol/L)
Mannitol	53 mg/dL (2.91 mmol/L)
Methyl-DOPA	1.5 mg/dL (0.07 mmol/L)
PAM iodide	80 mg/dL (3 mmol/L)
Pralidoxime Chloride	52 mg/dL (3 mmol/L)
Salicylate	60 mg/dL (4.34 mmol/L)
Sorbitol	600 mg/dL (33.5 mmol/L)
Sucrose	20 mg/dL (0.59 mmol/L)
Tolazamide	5 mg/dL (0.16 mmol/L)
Tolbutamide	64 mg/dL (2.37 mmol/L)
Triglyceride	3300 mg/dL (37.0 mmol/L)
Uric acid	23.5 mg/dL (1.40 mmol/L)
Xylitol	60.9 mg/dL (4 mmol/L)
Xylose	120 mg/dL (8.00 mmol/L)
α-Lipoic acid	2 mg/dL (0.10 mmol/L)

Conclusion

All the interferents tested passed the test at highest concentration except ascorbic acid. The instructions for use for the test strips contain the following statement in accordance with EN ISO 15197:2015, section 6.4.4.2:

"Interfering Substances: Results may be overestimated with abnormally high concentrations of ascorbic acid (vitamin C) > 3 mg/dl (0.17 mmol/l)".

User Performance Evaluation

The performance of the WaveSense JAZZ™ BGMS in the hands of the intended user was evaluated according to EN ISO 15197:2015, section 8.

Acceptance Criteria

Acceptance criteria for user performance evaluation are specified in EN ISO 15197:2015, section 8.2 as below:

95% of the individual glucose measured values shall fall within ± 0.83 mmol/l (± 15 mg/dl) of the measured values of the manufacturer's measurement procedure at glucose concentrations < 5.55 mmol/l (< 100 mg/dl) and within ±15% at glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl).

Method

172 Lay persons representing different ages, genders and educational levels were enrolled in the study. Blood glucose readings obtained by the lay user were compared to plasma glucose measured with the YSI 2300 STAT Plus reference method. The blood sample for the reference reading was obtained by a second finger stick performed by the technician. One lot of test strips was used in the study.

Results

The finger stick blood glucose results obtained by the user with the BGMS were compared against the reference plasma glucose determined by YSI 2300. The system accuracy difference plot is shown in Figure 4.

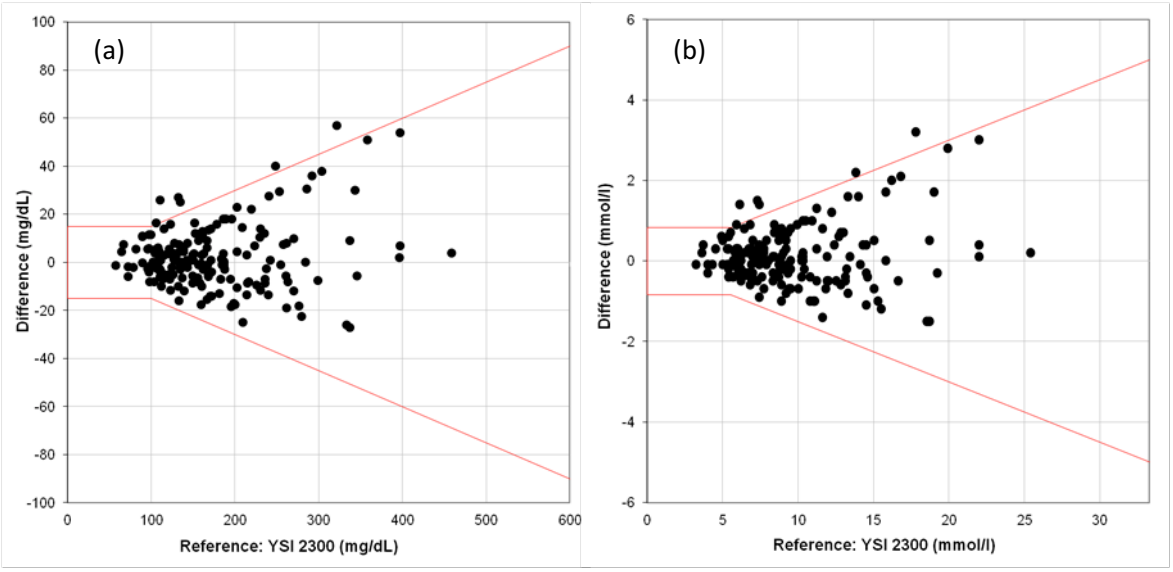

Figure 4: System accuracy plot – BGMS glucose vs. YSI 2300 plasma glucose concentration (User Study), (a) mg/dL and (b) mmol/l

The total number of acceptable results, i.e., individual glucose readings falling within ± 0.83 mmol/l (±15 mg/dl) of the measured values of the manufacturer's measurement procedure at glucose concentrations < 5.55 mmol/l (<100 mg/dl) and within ±15% at glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl), for all glucose concentrations was 166/172 (96.5.%). Also, 100% of the data (172/172) fall within zone A, defined as "no effect on clinical action" (2).

Table 3: User study, system accuracy results

User Study results for glucose concentrations < 5.55 mmol/l (< 100 mg/dl)		
Within ± 0.28 mmol/l (± 5 mg/dl)	**Within ± 0.28 mmol/l (± 5 mg/dl)**	**Within ± 0.28 mmol/l (± 5 mg/dl)**
8/18 (44.4%)	14/18 (77.8%)	18/18 (100%)
User Study results for glucose concentrations ≥ 5.55 mmol/l (≥ 100 mg/dl)		
Within ±5%	**Within ±10%**	**Within ±15%**
86/154 (55.8%)	133/154 (86.4%)	148/154 (96.1%)
User Study Results for glucose concentrations combined, using EN ISO 15197:2015 criteria		
Within ± 0.83 mmol/l (± 15 mg/dl) and ±15%		
166/172 (96.5.%)		

Conclusion

The WaveSense JAZZ™ blood glucose monitoring system meets the requirements for user performance evaluation in the EN ISO 15197:2015 standard.

Technical and Analytical Information

Specifications of the WaveSense JAZZ™ Blood Glucose Monitoring System	
Measurement principle	Glucose oxidase; indication by Dynamic Electrochemistry™
Measurement range	1.1 – 33.3 mmol/l (20 – 600 mg/dl)
Calibration	Plasma Equivalent
Measurement duration	5 seconds
Operating temperature range	10° - 40°C
Coding test strips	No coding required
Sample volume	0.5 µl
Strip shelf life	21 months (stored at 8°C to 30°C) unopened and 180 days after first opening
Haematocrit range	20-60%
Maximum altitude for measurement	3,048 meters
Operating Humidity	up to 90%
Sample Material	Capillary whole blood

Test Principle

The JAZZ test strip contains glucose oxidase (GOx) enzyme with a redox chemical mediator that produces an electrochemical signal in proportion to the glucose concentration in the blood sample. The blood glucose meter measures this signal, using dynamic electrochemistry to correct for common analytical interferences such as haematocrit.

Dynamic Electrochemistry

Dynamic Electrochemistry involves making multiple measurements and re-adjusting the input stimulation signal in response to how the chemistry is progressing. This dynamic adjustment results in a much richer output signal that forms the basis for a "fingerprint" that the meter's algorithms can analyze to develop correction factors to minimize the distortion caused by the interfering factors, such as temperature, sample irregularity, haematocrit effect, test strip condition and abnormal test strip use.

Reagent Composition

The JAZZ test strip contains the enzyme glucose oxidase (*Aspergillus niger*) and the mediator hexaammineruthenium (III) chloride.

Calibration Traceability

The JAZZ blood glucose monitoring system is plasma calibrated. These meters are factory calibrated and further calibration by the user is not necessary for operation. The calibration is traceable to NIST (D-glucose) SRM 917c.

References

1. **International Organization for Standardization.** *In vitro diagnostic test systems - requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.*. EN ISO 15197:2015.

2. *A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose.* **Parkes, J.L., et al.** 2000, Diabetes Care, Vol. 23, pp. 1143-1148.

3. **Clinical and Laboratory Standards Institute.** *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition.* 2005. CLSI EP7-A2 (ISBN 1-56238-584-4).