

PERFORMANCE OF THE NEW CONTOUR[®] BLOOD GLUCOSE MONITORING SYSTEM WITH CAPILLARY BLOOD



CONTOUR[®] Blood Glucose Monitoring System

ABSTRACT

The new CONTOUR[®] Blood Glucose Monitoring System (BGMS) provides results in five seconds, requires a sample volume of 0.6 μ L, has a memory capacity for 480 results, and takes advantage of technology that compensates for the effect of hematocrit. The flavin adenine dinucleotide (FAD) - glucose dehydrogenase (GDH) - based test strip chemistry eliminates interference by maltose*, making the CONTOUR BGMS suitable for peritoneal dialysis patients using icodextrin or patients receiving immunoglobulin preparations containing maltose.

Evaluations of the user guide and system performance with capillary blood specimens were conducted in two clinical studies by 184 subjects with diabetes. Healthcare professionals (HCP) tested subjects' blood in parallel. The studies assessed how well subjects, unfamiliar with the system and

*The FAD-GDH-based chemistry also eliminates interference by galactose.

using only the product labeling materials for instruction, could perform a finger puncture and obtain an accurate blood glucose result with the CONTOUR BGMS.

Meters referenced to plasma laboratory glucose methods and three test strip lots were used. Results obtained with the CONTOUR BGMS were compared to laboratory glucose values.

Ease of Use and Acceptability. Over ninety-nine percent (99.4%) of the subjects correctly performed a blood glucose test using the instructions accompanying the product. Subject ratings of the CONTOUR BGMS ranged from an average of 3.1 to 3.9 on a scale of 0.0 to 4.0 (0 = unacceptable, 1 = Poor, 2 = Good, 3 = Very Good, and 4 = Excellent). Ninety-six percent (96.2%) of the subjects stated that the CONTOUR BGMS would meet their needs, and 95.1% indicated that the system was easy to use.

Blood Glucose Testing. Analytical accuracy of combined lot data was statistically indistinguishable from data obtained with laboratory glucose analyzers. Agreement within ISO 15197:2003 accuracy limits of ± 15 mg/dL or 20% of the laboratory glucose result was >96% for lay subject and HCP operators.

Clinical accuracy was demonstrated by $\geq 97\%$ of subject or HCP results falling within Zone A when the data were examined by error grid analysis. No results were inside Zones C, D, or E.

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INTRODUCTION

The new CONTOUR[®] Blood Glucose Monitoring System (BGMS) system now provides results in five seconds, requires a sample volume of 0.6 µL, has a memory capacity for 480 results, and takes advantage of technology that compensates for the effect of hematocrit. The flavin adenine dinucleotide (FAD) - glucose dehydrogenase (GDH) - based test strip chemistry also eliminates interference by maltose*, making the BGMS suitable for peritoneal dialysis patients using icodextrin or patients receiving immunoglobulin preparations containing maltose.

Like its predecessor, the new CONTOUR BGMS is self-coding and automatically detects a control solution result, preventing the value from being used in the 14-day average calculation. In addition to the 14-day average, the new system provides other blood glucose tracking data, pre- and post-meal markers, and an alarm to remind the user to test their blood glucose after a meal.

Two clinical trials using fingerstick capillary blood were conducted to evaluate the clarity of the User Guide and Quick Reference Guide and system performance using multiple test strip lots. Both studies examined how well subjects, unfamiliar with the system and using only the User and Quick Reference Guides for instruction, could obtain an accurate blood glucose result. Blood glucose results obtained by untrained lay users were compared to data obtained by health care professionals (HCP) testing the subjects' blood in parallel. The measurements obtained by both lay and professional operators were compared to results obtained with a laboratory glucose analyzer.

The subjects rated features of the CONTOUR BGMS and answered questions about the system.

STUDY DESIGN AND METHODS

Protocols and Diabetes Centers

The evaluations were conducted at two diabetes centers in the Midwest (USA). One hundred

eighty-four subjects with diabetes completed the studies. Institutional Review Board approval of the protocol and informed consent were obtained from all subjects.

Labeling Comprehension Assessment for Performing a Blood Glucose Test. Subjects read the User and Quick Reference Guides, performed control solution assays, a finger puncture, and a blood glucose assay. The HCP assigned a proficiency rating based on the subject's ability to perform the procedures during the session. When the subjects felt ready, control solution and blood glucose measurements were performed to assess system performance and the subject's ability to obtain accurate blood glucose results using only the instructions provided in the labeling.

Subjects at Site 1 (n = 75) also performed functions related to meter set up, meal marking, memory, and battery replacement. All subjects completed a short questionnaire on the BGMS.

BGMS Performance. Three test strip lots were evenly distributed among the subjects at Site 1 who performed a self-finger puncture and two blood glucose assays. The HCP followed the regimen by performing a finger puncture on the subject and two blood glucose assays using the test strip lot assigned to the subject and an HCP dedicated meter.

Subjects at Site 2 (n = 109) evaluated the three test strip lots concurrently. The HCP tested in parallel, using the same test strip lot but with an HCP dedicated meter. A new finger puncture was performed between measurements with each lot.

Subjects performed duplicate control solution assays with each of three control levels (low, normal, and high) and the strip lot assigned to them (Site 1) or with each of the test strip lots (Site 2) in order to assess precision. HCPs performed assays with each of the three test strip lots one time each day on days that subjects were scheduled for visits.

Approximately half of the subjects evaluated the system at home for seven to 10 days to assess the robustness of the system, performing one normal

* The FAD-GDH-based chemistry also eliminates interference by galactose.

control solution assay and duplicate blood glucose measurements two times each day. The subjects returned to the clinic and repeated the initial visit testing regimen.

Sample Processing for Glucose and Hematocrit Determinations. After the BGMS measurements were performed, the HCP performed a deep fingerstick on the subject using a Tenderlet[®] (International Technidyne Corp.) or similar lancing device. Capillary blood was collected in a Microtainer[®] blood collection tube (Becton Dickinson) containing lithium heparin and a gel separator for a laboratory plasma glucose assay. A sample for a spun micro-hematocrit was also collected. The blood collection tube was centrifuged using a benchtop centrifuge to separate the plasma from the red blood cells. The plasma was transferred to a capped micro-centrifuge tube and refrigerated or frozen until duplicate laboratory glucose analyses were performed.

The glucose analyses were performed in the central laboratory at Site 1 using an Olympus 640 analyzer. Measurements at Site 2 were made using a Yellow Springs Instruments (YSI) analyzer STAT 2300.

Glucose Results

Differences between BGMS and laboratory results were calculated using the convention presented in the ISO 15197:2003 International Standard¹. An absolute difference (mg/dL or mmol/L) was used for samples having glucose concentrations <75 mg/dL (4.2 mmol/L). A percent difference was calculated for samples having glucose concentrations ≥75 mg/dL (≥4.2 mmol/L).

Accuracy and Precision of the Laboratory Glucose Analyzers

A set of six control sera ranging in concentration from 25.8 to 613.7 mg/dL (1.4 to 34.1 mmol/L), assayed by a method traceable to the National Institute of Standards and Testing (NIST) and the Centers for Disease Control and Prevention (CDC) reference method², were used to document the accuracy of the laboratory glucose analyzer. The

controls were run in duplicate for five runs over at least three days prior to assaying subject samples and in duplicate one time each week that subject samples were measured for a minimum of 10 runs.

The grand means of the results for each of the six control levels were within 5 mg/dL (0.3 mmol/L) for the two levels with target values <75 mg/dL or 5% for levels with target values ≥75 mg/dL (four levels) of the target level, and the overall CVs were <5.0%. No corrections were applied to the BGMS data to compensate for analyzer bias.

Data Analysis

Precision. The precision of the laboratory glucose analyzer and the CONTOUR[®] BGMS was calculated using the formulae presented in Appendix C of NCCLS EP5-A, *Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline*³.

Regression Analysis, Accuracy Criteria, Clinical Significance. The relationship between the BGMS and the laboratory glucose analyzer results was determined using Passing and Bablok comparison analysis (Analyse-it[™] ver.1.71, Analyse-It Software LTD, Leeds, England, UK). The coefficient of determination (R^2) was determined from the Pearson correlation statistic (R).

Analytical accuracy of the glucose results was determined using the criterion given in ISO 15197:2003 where the percentage of results within ±15 mg/dL or 20% was determined. Error grid analysis⁴ was used to assess the clinical significance of the deviations of the BGMS results from the laboratory glucose results.

The effect of hematocrit on analytical accuracy was determined by correlating the differences between the BGMS and laboratory glucose results to the subject hematocrits using least-squares regression analysis (Microsoft[®] Excel).

RESULTS AND DISCUSSION

Subject Demographics

Subject demographic information is presented in **Table 1**. The subject composition was nearly

evenly distributed between males and females (42/58%) A variety of ages and educational levels was represented, with the majority of the subjects (>85%) having type 2 diabetes. Most (59%) tested their blood glucose two to four times each day.

Blood Sample Characterization

The glucose concentration of the 221 samples obtained in the two studies ranged from 58.5 to 397 mg/L (3.2 to 22.0 mmol/L), with a median glucose concentration of 129.5 mg/dL (7.2 mmol/L). The sample hematocrit values ranged from 31 to 59%, with a median of 43%.

Ease of Use: Labeling Comprehension, System Setup, and Operation of Features

Ability of Untrained Users to Correctly Test. HCP ratings of the subjects' ability to perform control solution assays, a self-fingerstick, and a blood glucose test are given in **Table 2**.

Over ninety-seven percent (97.7%, 173/177) of the subjects either did not require any assistance (82.5%) or were directed to re-read sections of the User or Quick Reference Guides (16.9%). Only 0.6% (1/177) incorrectly performed part of the testing regimen and were unaware of their error.

Ability of Untrained Users to Perform Setup and Utilize System Features. Results from assessing the labeling related to the meter set up features, result and meal marking functions, memory recall, and battery replacement show that four of the 28 tasks the subjects performed received a success rate of less than 100%.

Understanding the meaning of the check mark was the most difficult feature for the subjects to comprehend (89.0% success). This was followed by knowing the significance of the log book icon (94.7% success), turning off the audible alarm (98.6% success) and accessing the user setup mode for a second time (98.7% success).

Table 1.
Subject Demographic Data

Demographic	n = 184	
Age (yrs), Median []	20 to 75 [54]	
Sex		
	Female	105 (58%)
	Male	76 (42%)
	Not recorded	3
Type of Diabetes		
	type 1	25 (14%)
	type 2	151 (86%)
	Unknown / No entry	8 ----
Education		
	Less than high school	9 (5%)
	High school	53 (29%)
	Some college or tech. school	68 (37%)
	Undergraduate degree (BA, BS)	43 (23%)
	Graduate degree (MA, MS)	10 (5%)
	Doctorate or professional degree	1 (1%)
Years Having Diabetes, Median []	1 mo to 44 [4]	
	Unknown / no entry	2
Years BG Testing, Median []	0 to 29 [4]	
	Unknown / no entry	2
Frequency of Testing		
	5 to 10 times per day	16 (9%)
	2 to 4 times per day	108 (59%)
	1 time per day	36 (20%)
	Less than 5 times per week	23 (12%)
	No entry	1
Complications*		
	Retinopathy	3
	Nephropathy	1
	Neuropathy	8
	Visual impairment	3
	Hearing impairment	9
	Motor skill impairment	6
Personal BGMS		
	Accu-Chek® (Roche)	41
	Ascensia® (Bayer)	51
	BD Logic™ / Medtronic	4
	One Touch® (LifeScan)	54
	FreeStyle® (Abbott)	17
	Precision Xtra™ (Abbott)	1
	Not indicated / Other	16

*Multiple complications are listed separately.

One subject at Site 2 received glucose tablets for hypoglycemia. Blood glucose data from that subject were not used in the analysis, but demographic and control solution data were included.

Table 2.
Success Rate of Subjects Performing Control and Blood Glucose Testing

Rating	Description	% of Subjects
1	Performed all tests correctly <i>without assistance.</i>	82.5% (146/177)
2	Performed all tests correctly but was directed to a specific part of the User Guide / Quick Reference Guide by the HCP because of a subject's question.	16.9% (27/177)
3	Performed all tests correctly but required verbal assistance or review of a part of the User Guide / Quick Reference Guide.	1.7% (3/177)
4	Incorrectly performed part of the testing regimen and was unaware of the error. Required intervention by the HCP.	0.6% (1/177)

A rating was not recorded for one subject at Site 1 and for six subjects at Site 2.

Agreement of BGMS Results with Laboratory Blood Glucose Results

Statistics showing combined lot agreement of the CONTOUR[®] BGMS results with the laboratory glucose results are shown in **Table 3**.

Using the 95% confidence intervals of the slopes and intercepts, within-lot comparisons of HCP and lay user results showed no statistically significant difference by operator. Between-lot comparisons of results obtained by either HCP or lay users also did not show statistically significant differences.

The coefficients of determination (R^2) showed that about 94% of the BGMS variation from the laboratory results could be explained by the regression analysis.

Table 4 shows the agreement of HCP and lay-user results obtained with the CONTOUR BGMS with laboratory glucose results using ISO 15197:2003 accuracy criteria. Greater than 96% of the combined lot results met the accuracy criteria.

Table 4.
Agreement of CONTOUR[®] BGMS Results with Laboratory Glucose Analyzer Results Using ISO 15197:2003 Accuracy Criteria

Lot	Operator	Results within ± 15 mg/dL (4.2 mmol/L) or 20% of the Laboratory Glucose Analyzer*
Combined	HCP	96.8% (423/437)
	Lay	96.3% (421/437)

*ISO 15197:2003 Accuracy Criteria
HCP = Health Care Professional

Error Grid Analysis

Error grid analysis to determine the clinical accuracy of the blood glucose values obtained by lay and professional meter operators with combined test strip results is presented in **Table 5**.

Ninety-seven and 98% of the results were inside Zone A (no effect on clinical action), with the remaining values inside Zone B (altered clinical action with little or no effect on clinical outcome).

Table 3.
Relationship of CONTOUR[®] BGMS Results with Laboratory Glucose Results

Lot	n	Operator	y =	95% Confidence Interval		R^2
				Slope	Intercept	
Combined	437	HCP	0.98x + 1.95 mg/dL 0.98x + 0.1 mmol/L	0.95 to 1.00	-1.00 to 5.67 mg/dL -0.2 to 0.3 mmol/L	0.941
		Lay	1.00x - 1.50 mg/dL 1.00x - 0.1 mmol/L	0.97 to 1.03	-4.92 to 1.45 mg/dL -0.3 to 0.1 mmol/L	0.936

HCP = Health Care Professional

Table 5.
Error Grid Analysis of Blood Glucose Results
Obtained by Professional and Lay Users

Lot	n	User	Percentage of Results within Error Grid Zones		
			Zone A	Zone B	Zones C/D/E
Com- bined	437	HCP	98% (429/437)	2% (8/437)	0%
		Lay	97% (423/437)	3% (14/437)	0%

HCP = Health Care Professional

No results fell inside Zones C, D, or E (altered clinical action affecting clinical outcome).

The results obtained with each test strip lot are plotted in **Figure 1**. Scatter plots with the error grid and difference plots with ISO 15197:2003 accuracy limits are shown. Panels A and B show results obtained by lay-users. Panels C and D show results obtained by HCPs.

Effect of Hematocrit

Combined results obtained by lay user and HCP operators using the three test strip lots were evaluated to assess the effect of hematocrit on the CONTOUR[®] BGMS glucose results.

The percent difference of the BGMS value from the laboratory glucose value was plotted against the sample hematocrit (**Figure 2**). Regression statistics are given in **Table 6**.

Table 6.

Regression Statistics of the Relationship Between Hematocrit and the Percent Difference from the Laboratory Glucose Method with the CONTOUR[®] BGMS

n	y =	95% Confidence Interval		Sy•x	R ²
		Slope	Intercept		
868	0.23x - 10.62%	0.09 to 0.37	-16.76 to -4.47	9.20	0.011

The analysis showed a slight over-compensation for hematocrit that was statistically significant (95% confidence interval of the slope does not include zero), but clinically insignificant. Using the regression equation and theoretical hematocrit extremes of 20% and 70%, a sample hematocrit of 20% would give a 5.1% under-estimation of glucose, whereas a sample hematocrit of 70%

would give a 6.4% over-estimation of glucose from nominal hematocrit values of 42%.

Home-Use Testing

Home-use testing allowed subjects to use the CONTOUR BGMS in an unsupervised environment in order to assess the robustness of the system and to collect data for precision analysis. Precision data obtained with the normal control solution and fingerstick capillary blood were used to assess how well results generated outside the diabetes center compared to data obtained in the presence of an HCP. Accuracy was not assessed due to lack of a suitable comparative method.

The CVs and percentages of normal control results within the acceptable ranges for each test strip lot were comparable to those obtained at the diabetes centers, where the overall standard deviations of the low control results were <2.0 mg/dL (0.1 mmol/L) and CVs of the normal and high controls were <3.3% for lay or professional meter operators at each site. The percentage of results within acceptable ranges during home use testing for the three lots (n = 104, 118, 99) ranged from 97.5 to 100% (data not shown).

To assess precision with blood samples, average CVs were calculated from the variances of the replicates for sample groups with glucose concentrations <126 mg/dL (<7.0 mmol/L) and ≥126 mg/dL (≥7.0 mmol/L). Results obtained by subjects and HCPs during the initial and return visits are presented in **Table 7**. The home-use results compared favorably with results obtained at the diabetes centers.

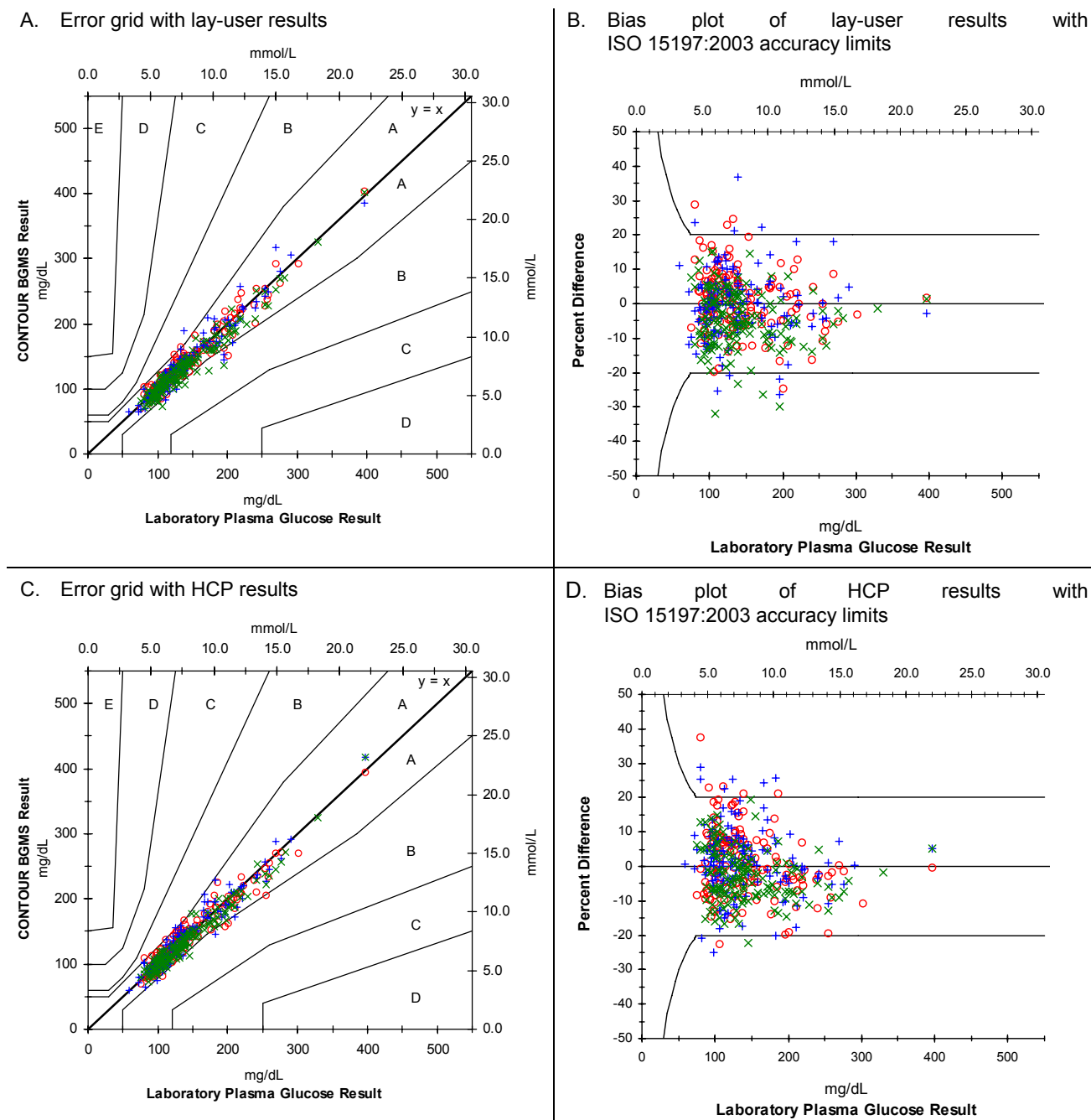
The data show that lay-users, with minimal training and using the system without the presence of an HCP, obtained results similar to those obtained by HCPs and lay-users at a diabetes clinic.

User Acceptability

The 184 lay subjects rated 26 aspects of the CONTOUR BGMS using a rating system of 0 (Unacceptable) to 4 (Excellent) and gave narrative feedback to several questions about the

Figure 1.

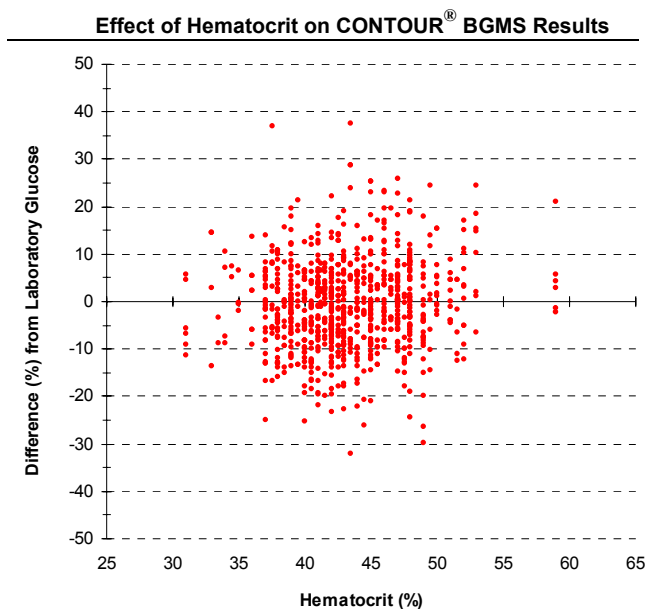
CONTOUR® BGMS Results Obtained by Lay and Professional Users Compared to Laboratory Glucose Results



Panels A, B, C, and D: ○ = Lot A (n = 147), + = Lot B (n = 145), × = Lot C (n = 145).

Panels B and D: Limits are the percentage of a ±15 mg/dL (0.8 mmol/L) difference at glucose concentrations <75 mg/dL (<4.2 mmol/L) and ±20% at glucose concentrations ≥75 mg/dL (≥4.2 mmol/L)

Figure 2.



Results from three samples (lay and professional operators) with glucose concentrations <75 mg/dL (4.2 mmol/L) are not presented.

system. Subject and HCP responses are presented in **Figure 3**.

The features are ranked in descending order by the mean of the subject response. The average subject ratings ranged from Very Good to Excellent. (3.1 to 3.9). The auto calibration feature received the highest subject rating (3.9). Auto calibration, the 5-second test time, and the auto control marking feature were all rated as Excellent (4.0) by the

HCPs. The size and appearance of the test strip bottle and the ease of removing a test strip from the bottle still received a Very Good rating but were rated at the lower end of the rankings by both subjects and HCPs.

The CONTOUR® BGMS was well received by the study subjects. Ninety-six percent (96.2%) of the subjects stated that the CONTOUR BGMS would meet their needs, and 95.1% indicated that the system was easy to use. A little over half (53.3%) indicated that the memory functions were easier to use than their current system, and 90.1% stated that the User Guide and Quick Reference Card were easy to understand. About 70% (73.7%) stated that they would switch from their current meter to the CONTOUR system.

SUMMARY AND CONCLUSIONS

Ninety-nine percent of untrained users obtained results that were analytically and clinically accurate using the User Guide and Quick Reference Card for instruction.

- Analytical accuracy was statistically indistinguishable from results obtained with laboratory glucose analyzers. Greater than 96% of results were within limits of ± 15 mg/dL or 20% of the laboratory glucose result.

Table 7.

Precision of the CONTOUR® BGMS Using Fingerstick Blood

Operator	Sample Blood Glucose*					
	<126 mg/dL (7.0 mmol/L)			≥126 mg/dL (7.0 mmol/L)		
	n	Mean	Avg. CV	n	Mean	Avg. CV
Initial and Return Visits						
HCP	43	100 mg/dL 5.6 mmol/L	10.0%	70	172 mg/dL 9.5 mmol/L	7.6%
Lay User	43	100 mg/dL 5.6 mmol/L	10.0%	70	172 mg/dL 9.5 mmol/L	7.6%
Lay User at Home	288	105 mg/dL 5.8 mmol/L	7.30%	328	166 mg/dL 9.2 mmol/L	7.4%

* Selection for the sample blood glucose concentration bin was determined by the value of the first replicate obtained by the subject.

- Clinical accuracy, assessed by error grid analysis, was excellent. Greater than 97% of results were within Zone A (no effect on clinical action). No results were inside Zones C, D, or E. Results falling in these areas could lead to incorrect clinical decisions.
- Hematocrit compensation eliminated the effect of under-estimation of glucose at high hematocrit values, a phenomenon found with many BGMS.
- Greater than 95% of control results were within the acceptable control range. Precision with control solutions was excellent, with coefficients of variation $\leq 3.0\%$.
- Home-use testing data showed that the system was robust. Lay-users, with minimal training, obtained results similar to those generated by HCPs and lay-users in a diabetes clinic.

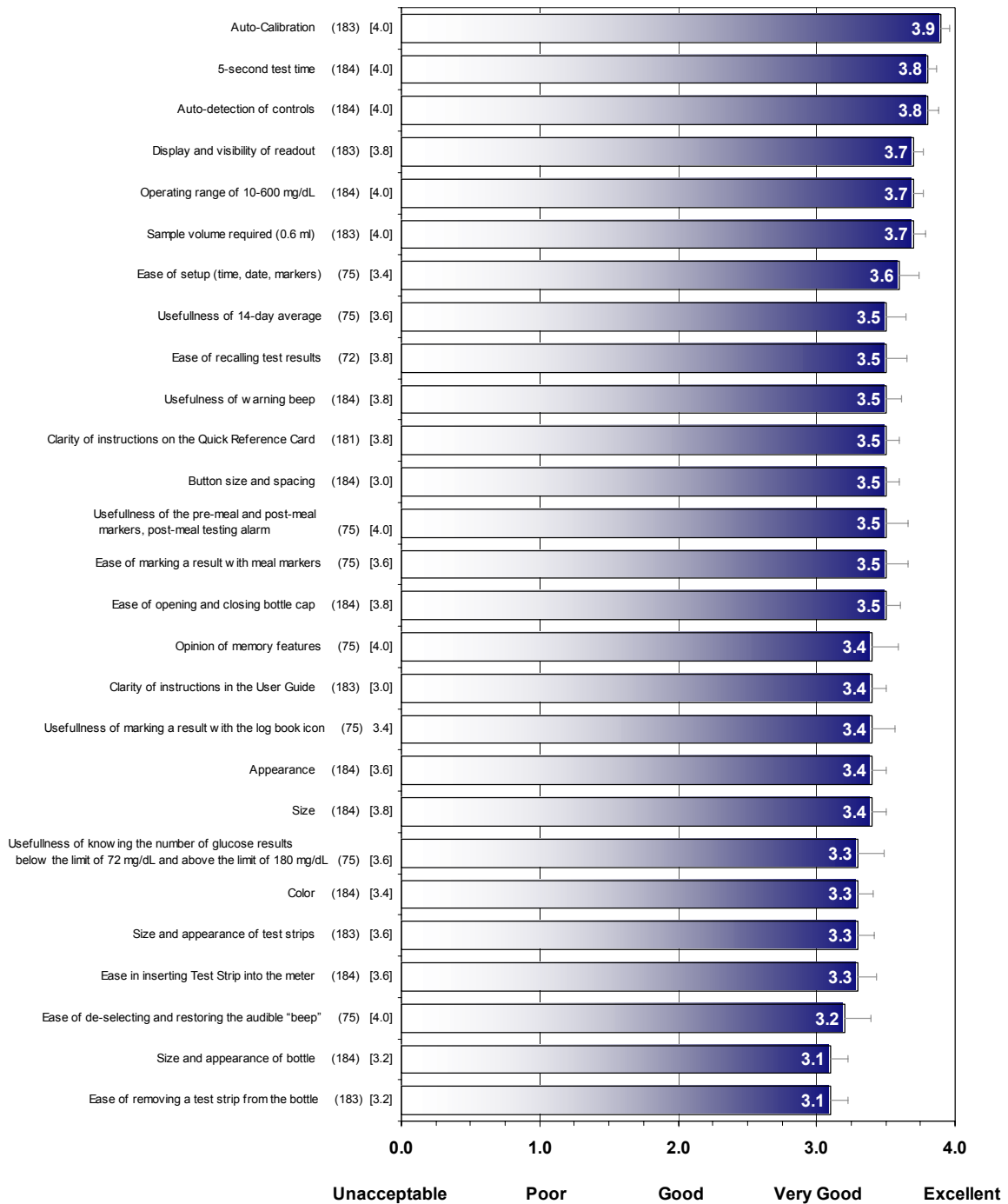
The new CONTOUR[®] BGMS was well received by the study subjects. The average ratings of the system and its features ranged from Very Good to Excellent.

REFERENCES

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Figure 3.

Ratings of CONTOUR® BGMS Features by Study Subjects and Site Professional Staff



Average ratings by site staff (n = 5) are in brackets []. Average subject ratings and 95% confidence intervals of the mean are at the end of the bars. The number of subject responses are in parentheses ().

