Clinical Evaluation of a Faster, Smaller Volume Blood Glucose Test Strip Based on TrueMeasure™ Technology

Executive Summary

Objective:

To evaluate the clinical performance of a new (0.6 µL, 5-second) blood glucose test strip, based on TrueMeasure technology, for use with the Precision Xceed™ and Optium Xceed™ meters for fingertip and alternative site testing.

Method:

To assess user performance, capillary blood glucose testing on the fingertip and three alternative sites (forearm, upper arm and palm) using the new test strip was evaluated at four diabetes clinics with multiple lots of the test strip. Results were compared to the YSI plasma equivalent glucose values of the fingertip blood. Subjects participating in these studies were also asked to assess ease of use. Additional laboratory studies were performed at Abbott Diabetes Care Inc. to validate performance under various testing conditions.

Results:

In the fingertip study conducted at 2 diabetes clinics, accuracy of the new test strip was demonstrated by comparing results from 108 patients with the YSI plasma equivalent glucose values ($r = 0.97$, mean absolute bias = 7.4 %). Ninety-seven percent of the test strip results agreed within ± 15 mg/dL (± 0.83 mmol/L) of the YSI values at glucose concentrations < 75 mg/dL (4.2 mmol/L) and within ± 20% at glucose concentrations ≥ 75 mg/dL (4.2 mmol/L). One hundred twenty-three patients were surveyed on the ease of use with the new test strip for fingertip testing. Using a rating scale of 1 to 6 (6 reflecting the greatest ease), the overall mean rating by 123 patients was 5.4, indicating that these first-time users found the new test strip easy to use.

At another 2 diabetes clinics, alternative site testing results obtained with the new test strip by 96 lay users correlated well ($r \geq 0.91$) with those obtained by the trained operators. When compared to the fingertip blood glucose values from the YSI Analyzer, 100% of the alternative site test results obtained by the lay users fell within zones A and B of the Consensus Error Grid, indicating clinical acceptability. In the ease-of-use survey based on a rating scale of 1 to 6 (6 reflecting the greatest ease), the overall mean rating by first-time users was 5.2, indicating that the patients found the new test strip easy to use for alternative site testing. In the pain rating survey, 95% of the users found testing on the arm with the new test strip completely or virtually painless.

In the laboratory studies, precision of the new test strip, determined as coefficients of variation (CV), ranged from 2.5% to 4.3%. The new test strip produced accurate results at high altitude (7,200 feet or 2,195 metres above sea level), across a haematocrit range of 30-55% and a glucose measurement range of 20-500 mg/dL (1.1-27.8 mmol/L), and with a minimum sample volume of 0.6 µL (calculated based on the dimensions of the cell that holds the sample in the strip). Additional studies showed that the following produced no clinically significant effect on the accuracy of the new test strip: meter movement, second blood drop application within 5 seconds, various sample application techniques, various sample volume applications and numerous drugs and endogenous substances at high concentrations.

Conclusions:

In the clinical studies, accuracy and ease of use of the new (0.6 µL, 5-second) TrueMeasure technology test strip for fingertip and alternative site testing were verified by more than 200 lay users. Additional studies demonstrated that the new test strip maintained accuracy in various challenging conditions that may be encountered in everyday home testing and it received a high ease-of-use rating by first-time users.

Abbott
A Promise for Life

A new biosensor test strip, based on TrueMeasure technology, has been developed for use with the Precision Xceed and Optium Xceed meters. This test strip allows the user to apply blood to either the top or the end of the test strip. The blood is automatically drawn into the reaction area. The sample volume requirement is 0.6 µL and test time is 5 seconds. Multicenter studies were conducted to evaluate user performance and ease of use. Additional studies were performed to validate performance claims under various testing conditions

Materials and Methods

Test Method

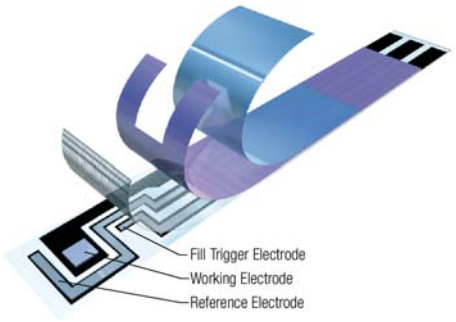
The new biosensor test strip is based on Abbott TrueMeasure technology. Glucose in the blood specimen reacts with a NAD-requiring glucose dehydrogenase (GDH-NAD) on the test strip. This chemical reaction releases electrons, which are transferred from the enzyme to the electrodes by a mediator. These electrons generate a small current, which is proportional to the concentration of glucose in the specimen and measured by the meter. The analysis time is 5 seconds.

The new test strip (*Figure 1*) contains three electrodes (working, reference, and fill trigger electrodes). The circuit between the fill trigger and reference electrodes must be detected by the meter before the test will start. This can occur only when the applied sample flows beyond the reference and working electrodes to contact the fill trigger electrode. The fill trigger electrode is designed to minimize the potential for errors that may occur when not enough blood is applied to the test strip and to reduce wasting of test strips.

Upon application of sufficient blood sample, the test is automatically initiated. Glucose dehydrogenase (GDH-NAD) and an electron mediator (PQ) are present on the working electrode of the test strip. The GDH catalyzes the oxidation of glucose to gluconolactone by accepting two electrons from a glucose molecule, and the GDH is reduced. The oxidized form of the electron mediator accepts the electrons from the reduced GDH, thus the mediator is reduced and the enzyme returns to its oxidized state. The reduced mediator is oxidized at the working electrode, which produces a small electric current proportional to the glucose concentration in the sample. In this electrochemical reaction, a low applied potential is used to minimize interference by reducing substances such as vitamin C, uric acid and acetominophen; GDH-NAD is used to avoid interference by certain carbohydrates such as maltose (in patients dialyzed with icodextrin-containing solution).

The combination of the fill-trigger and the GDH-NAD based chemistry with a low applied electric potential is the basis of TrueMeasure technology, designed to minimize errors from insufficient blood samples and interfering substances.

Figure 1. The New TrueMeasure Technology Test Strip



$$\text{Glucose} + GDH_{(ox)} \longrightarrow \text{Gluconolactone} + GDH_{(red)}$$

$$GDH_{(red)} + NAD^{+} \longrightarrow GDH_{(ox)} + NADH$$

$$NADH + PQ_{(ox)} \longrightarrow NAD^{+} + PQH_{2(red)}$$

$$PQH_{2(red)} \xrightarrow{+\ 200\ mV} PQ_{(ox)} + \text{electrons (e-)}$$

Comparative Methods

The YSI 2300 Stat Plus Glucose Analyzer (YSI Inc., Yellow Springs, OH) was used as the comparative method at all clinical study sites. The YSI whole blood glucose results were multiplied by 1.12 to yield plasma equivalent values.

User Performance Studies

Fingertip Testing

User performance of the new test strip was evaluated at 2 diabetes clinics. Two lots of test strips were used at each clinic; each strip lot was used by approximately half of the subjects. One hundred twenty-three subjects enrolled in the study. Fifteen subjects were excluded due to protocol deviations yielding 108 subjects. Fingertip capillary blood glucose results obtained with the new test strip were compared to results obtained on the YSI.

Alternative Site Testing

At another 2 diabetes clinics, testing on the forearm, upper arm and palm were evaluated, using two lots of test strips. Both lots were used on approximately half the subjects. A total of 120 subjects participated in the study. Twenty-four subjects were excluded due to protocol deviations yielding 96 subjects. Alternative site testing results obtained by the subjects with the new test strip were compared to those obtained by the trained healthcare professionals and to fingertip glucose results obtained on the YSI.

Ease-of-Use Surveys

In the user performance studies, a total of 123 patients at two diabetes clinics evaluated fingertip testing and 120 patients at another two diabetes clinics evaluated alternative site testing. These lay users performed the tests on their own after reading the instructions for use. They were asked to complete a questionnaire rating various ease-of-use topics including handling of the test strips and application of blood specimens. A scale of 1 to 6 was used, with a rating of 6 reflecting the greatest ease. An overall ease-of-use rating was obtained by averaging all responses for each study.

Pain Rating

A total of 82 lay users at two diabetes clinics participated in the pain rating survey for arm testing. After performing testing on their arms, these lay users were asked to rate the pain of testing.

Laboratory Studies

The following studies were performed at Abbott Diabetes Care Inc.

Precision

Precision of the new test strip was assessed at five glucose levels by analyzing heparinized venous blood in 20 successive replicates. Three lots of test strips were used. For the lowest glucose level (less than 60 mg/dL or 3.33 mmol/L), the standard deviation values were averaged across the three lots. For the other four glucose levels, the coefficient of variation (CV) values of the three lots were averaged.

Sample Volume Requirements

The sample volume requirement is calculated based on the dimensions of the cell that holds the sample in the test strip. Testing below 1.0 µL is limited by the lack of an accurate and reproducible method for dispensing blood at various volumes in the sub-microliter range. The effect of sample volume on the performance of the new test strip was evaluated by applying 0.5, 1.0 and 3.0 µL of venous blood to the test strips. Three concentrations of glucose were tested on three different days with three lots of test strips. Twenty-four replicates of testing were performed each day for each sample volume and glucose level. For each sample volume, glucose level and test strip lot, the difference in mean bias or mean percent bias between each volume and the control volume (3 µL) was calculated.

Effect of Meter Movement

The effect of performing testing while holding the meter was evaluated with three lots of the new glucose test strip using capillary blood samples. On each of two days, twenty subjects tested their own fingertip blood specimens in duplicate with all three lots of test strips using an equal number of meters which were hand-held and meters that remained stationary on a flat surface (control condition) throughout the experiment. The difference in percent bias between the test conditions and the control was calculated for each sample and test strip lot and examined for clinical significance.

Effect of Haematocrit

Three lots of the new glucose test strips were tested with venous blood adjusted to four glucose concentrations (approximately 50, 90, 350 and 396 mg/dL; 2.8, 5.0, 19.4 and 21.9 mmol/L) and six haematocrit levels (30, 35, 40, 45, 50 and 55%). Twelve consecutive tests were performed at each level of glucose and haematocrit on each test strip lot, with the exception of the control condition samples (45% haematocrit), which were analyzed in 24 replicate measurements. The difference in mean bias [for glucose ≤ 75 mg/dL (4.2 mmol/L)] or mean percent bias [for glucose > 75 mg/dL (4.2 mmol/L)] between the test conditions and the control condition (45% haematocrit) was calculated for each glucose level, haematocrit, and test strip lot number.

Interference Studies

Sixty-seven substances, at concentrations much higher than normal or therapeutic levels, had been tested for interference on two previous versions of the TrueMeasure technology test strip. Only xylose, at high concentrations found only during xylose absorption test, interfered by producing elevated glucose results. Differences in the designs between the new test strip and the two previous versions may influence the resistance to interference from 25 of the 67 substances, based on their biochemical and electrochemical properties. Thus, those 25 substances were tested on the new test strip. Venous blood samples adjusted to a glucose concentration of 100 mg/dL (5.5 mmol/L) were divided into two portions: a test sample and a control sample. A concentrated solution of the substance was added to the test sample and an equal volume of the solvent that was used to dissolve the substance was added to the control sample. Paired-difference testing was conducted on each sample with twenty-four assays for each of three test strip lots. An interfering substance is defined as one that produces a bias greater than 6 mg/dL (0.33 mmol/L) from the control sample in the paired-difference testing and is confirmable by dose-response testing at varying concentrations of the interfering substance.

Effect of Sample Re-Application

Three lots of the new glucose test strip were tested over three days at three glucose concentrations (approximately 50, 90, and 350 mg/dL; 2.8, 5.0, and 19.4 mmol/L). An initial sample volume of 0.5 µL followed by a second sample of 3.0 µL, was applied at two different time delays (2 and 5 seconds). Twelve consecutive tests were conducted on each day for each test strip lot number, time delay, and glucose level with the exception of the control condition, where 24 replicate assays were performed. The difference in mean bias [for glucose ≤ 75 mg/dL (4.2 mmol/L)] or mean percent bias [for glucose > 75 mg/dL (4.2 mmol/L)] was calculated for each test strip lot between each test condition and the control condition (a single 3 µL drop).

Effect of Sample Application Technique

Three lots of the new glucose test strip were evaluated with 20 donors over four days using four different blood application methods: (1) hanging drop (control method), (2) touching the finger to the test strips during application (3) smearing the finger lightly over the target area of the test strip during application and (4) end fill or applying the blood at the end of the test strip. Twenty assays in duplicate were conducted on days 1 and 2 for hanging drop, touching and smearing methods and on days 3 and 4 for hanging drop and end fill. The mean percent bias between the different application methods and the control condition was calculated and averaged over the three batches.

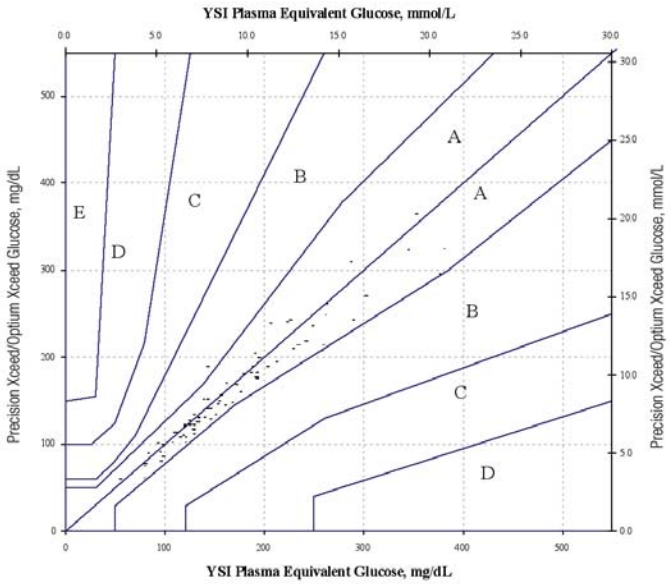
Results

User Performance Studies

Fingertip Testing

The new test strip provided accurate results in fingertip testing (Figure 2). Good correlation was found between test strip results and comparative method results (r = 0.97; slope = 0.92 and intercept = 5.8 mg/dL [0.32 mmol/L] by regression analysis; mean absolute percent bias = 7.4 %; n = 108 tests). Ninety-seven percent of the test strip results agreed within ±15mg/dL (0.83 mmol/L) of the YSI values at glucose concentrations < 75 mg/dL (4.2 mmol/L) and within ± 20% at glucose concentrations ≥ 75 mg/dL (4.2 mmol/L). Of the 108 test results, 104 (96.3 %) were in Zone A (clinically accurate) and 4 (3.7%) were in Zone B (clinically acceptable) of the Consensus Error Grid[1]. The haematocrit range of the capillary blood specimens in this study was 33-52%.

Figure 2. Fingertip Testing by 108 Lay Users



Zone A: Clinically accurate (no effect on clinical action)
Zone B: Clinically acceptable (altered clinical action—little or no effect on clinical outcome)
Zone C: Altered clinical action—likely to effect clinical outcome
Zone D: Altered clinical action—could have significant medical risk
Zone E: Altered clinical action—could have dangerous consequences

Alternative Site Testing

Even though the results of different blood samples were compared (test strip results on alternative site blood samples vs. YSI results on fingertip blood samples), good agreement was found between alternative site results obtained by lay users with the new test strip and YSI fingertip results (slope = 0.96, intercept = 6 mg/dL [0.33 mmol/L], n = 96). Consensus error grid analysis showed that 89% and 11% of the alternative site test results by the lay users fell within Zones A and B, respectively *(Table 1)*.

[1] Parkes JL, Pardo S, Slatin SL, Ginsberg GH. A new consensus error grid to evaluate the clinical significance of inaccuracies in the measurement of blood glucose. *Diabetes Care* 2000;23:1143-1148.

Table 1. Consensus Error Grid Analysis of the New Glucose Test Strip for Alternative Site Testing by 96 Lay Users

Percentage of Test Strip Results in Zone	Zone A	Zone B	Zone C	Zone D	Zone E
All tests n = 96	89	11	0	0	0

Zone A: Clinically accurate (no effect on clinical action)
Zone B: Clinically acceptable (altered clinical action—little or no effect on clinical outcome)
Zone C: Altered clinical action—likely to effect clinical outcome
Zone D: Altered clinical action—could have significant medical risk
Zone E: Altered clinical action—could have dangerous consequences

Ease-of-Use

Fingertip Testing

One hundred twenty-three lay users at 2 study centers completed a questionnaire rating the new test strip for ease-of-use for fingertip testing. A scale of 1 to 6 was used, with 6 reflecting the greatest ease. An overall ease-of-use rating of 5.4 was obtained when all responses were averaged, indicating that the lay users found the new test strip easy to use *(Table 2)*.

The ages of the lay users ranged from 20 to 81 years old. Fifty percent of the subjects were male and 50% were female. Their education levels spanned from grade school to post graduate degrees. Seventeen percent had type 1 diabetes and 83% had type 2 diabetes.

Table 2. Ease-of-Use Rating of the New Glucose Test Strip for Fingertip Testing by 123 Lay Users

Statement	Mean Rating The rating scale is 1 to 6 for each statement; (6 reflecting greatest ease).
The size of the test strip is adequate	5.4
The test strip is easy to handle	5.2
It is easy to insert the test strip	5.7
It is easy to identify the sample application area	5.4
It is easy to apply blood	5.3
I had enough time to apply blood	5.7
The test is quick	5.5
The test strip is convenient	5.0
The test strip is easy to use	5.3
The test instructions were easy to follow	5.5
Overall Mean	**5.4**

Alternative Site Testing

One hundred twenty lay users at 2 study centers completed a questionnaire rating the new test strip for ease-of-use for alternative site testing. A scale of 1 to 6 was used, with 6 reflecting the greatest ease. An overall ease-of-use rating of 5.2 was obtained when all responses were averaged, indicating that the lay users found the new test strip easy to use *(Table 3)*.

The ages of the lay users ranged from 23 to 82 years old. Fifty one percent of the subjects were male and 49% were female. Their education levels spanned from junior high to post graduate degrees. Eleven percent had type 1 diabetes and 89% had type 2 diabetes.

Table 3. Ease-of-Use Rating of the New Glucose Test Strip for Alternative Site Testing by 120 Lay Users

Statement	Mean Rating* The rating scale is 1 to 6 for each statement; (6 reflecting greatest ease).
Easy-to-learn	5.5
Easy-to-use	5.0
Overall Mean	**5.2**

Pain Rating

Eighty two lay users at 2 study centers completed a questionnaire rating the pain of testing with the new test strip. Ninety five percent of lay users found arm testing with the new test strip to be completely or virtually painless *(Table 4)*.

Table 4. Pain Rating of the New Glucose Test Strip for Arm Testing by 82 Lay Users

Statement	Number (Percent) of users who selected response
Completely painless	38 (46%)
Virtually painless	40 (49%)
Slight pain	3 (4%)
Moderate pain	1 (1%)
Severe pain	0 (0%)

Laboratory Testing

Precision

In the precision study using three lots the new glucose test strip and fresh venous blood samples, the standard deviation (SD) was 2.0 mg/dL (0.11 mmol/L) for glucose < 60 mg/dL (3.33 mmol/L) and the coefficient of variation (CV) ranged from 2.5 to 3.2% for glucose ≥ 60 mg/dL (≥ 3.33 mmol/L) (Table 5).

Table 5. Precision

Mean mg/dL (mmol/L)	46.5 (2.6)	86.8 (4.8)	135.7 (7.5)	198.5 (11.0)	320.1 (17.8)
SD	2.0 (0.11)				
CV, %	4.3	3.0	2.7	2.5	3.2

Sample Volume Requirements

The sample volume of the new test strip is 0.6 µL. This is calculated based on the dimensions of the cell that holds the sample in the test strip. In this study, the various sample volumes tested gave clinically acceptable results on the three lots of new test strips. None of the tests started at 0.5 µL. Compared to the control volume (3.0 µL), all mean biases at 1.0 µL were less than 2 mg/dL (0.11 mmol/L) or 3% *(Table 6)*.

Table 6. Effect of Sample Volume

Glucose*, mg/dL (mmol/L)	Mean Bias (mg/dL, mmol/L or %) vs. the Control Volume (3.0 µL)	
	0.5 µL	**1.0 µL**
50 (2.8)	Did not start	-1.17 mg/dL, -0.06 mmol/L
90 (5.0)	Did not start	2.7%
350 (19.4)	Did not start	-1.1%

*Approximate concentrations.

Effect of Meter Movement

The effect of performing the testing while holding the meter in the hand was evaluated with three lots of the new glucose test strips. On each of two days, twenty capillary samples were tested using equal numbers of meters which were (1) hand held and (2) remained stationary throughout the experiment. The difference in mean percent bias between the stationary and hand held results was less than 0.5%, thus there was no clinically significant difference between the two testing conditions.

Effect of Haematocrit

Three lots of the new test strips were tested at four glucose concentrations (approximately 50, 90, 350 and 396 mg/dL; 2.8, 5.0, 19.4 and 21.9 mmol/L) and six haematocrit levels (30, 35, 40, 45, 50 and 55%). For each lot at each level of glucose and haematocrit, the mean bias/mean % was within 6.0 mg/dL (0.33 mmol/L) or 16% of the control condition (45% haematocrit), indicating clinically acceptable performance across a haematocrit range of 30-55%.

Interference Studies

Of the twenty-five substances tested at high concentrations in this study, only xylose interfered with the new test strip. Table 7 lists all substances tested to date. Dose response testing for xylose indicates that xylose may produce elevated results only during a xylose absorption test for diagnostic evaluation of malabsorption. This finding is consistent with those on the previous versions of the TrueMeasure technology test strip.

*Table 7. Substances Tested for Interference with TrueMeasure Technology Test Strips**

Substance	Upper Limit of Therapeutic or Normal Concentration		Concentration Tested	
Exogenous				
Acarbose (Glucobay)	-	-	120 mg/dL	1859 µmol/L
Acetaminophen (Tylenol)	3 mg/dL	199 µmol/L	25 mg/dL	1655 µmol/L
Amoxicillin	-	-	345 mg/dL	9441 µmol/L
Ampicillin	0.5 mg/dL	14 µmol/L	5 mg/dL	143 µmol/L
Ascorbic Acid (Vitamin C)	1.5 mg/dL	85 µmol/L	4 mg/dL	227 µmol/L
Captopril (Lopirin)	-	-	90 mg/dL	4140 µmol/L
Cefaclor (Ceclor)	0.7-2.3 mg/dL	-	23 mg/dL	596 µmol/L
Chlorpropamide (Diabinese)	14 mg/dL	506 µmol/L	75 mg/dL	2710 µmol/L
Citric Acid	-	-	30 mg/dL	156 µmol/L
Diazoxide	-	-	75 mg/dL	325 µmol/L
Digoxin	1.2 ng/mL	1.3-2.6 nmol/L	100 mg/dL	1,280 µmol/L
Diltiazem (Cardizem)	0.02 mg/dL	0.44 µmol/L	75 mg/dL	1663 µmol/L
Dopamine	0.03 mg/dL	1.96 µmol/L	0.09 mg/dL	5.88 µmol/L
Enalapril (Vasotec)	-	-	8 mg/dL	162 µmol/L
Ephedrine	1.8 mg/dL	89 µmol/L	5.4 mg/dL	267 µmol/L
Ethanol	100 mg/dL	22 mmol/L	400 mg/dL	86.8 mmol/L
Ethinylestradiol	-	-	20 mg/dL	675 µmol/L
Fluoxetine (Prozac)	-	-	4 mg/dL	116 µmol/L
Gentisic Acid	0.6 mg/dL	39 µmol/L	1.8 mg/dL	117 µmol/L
Glibenclamide/Glyburide	-	-	0.25 mg/dL	5 µmol/L
Gliclazide (Diamicron) Nordialex)	-	-	32 mg/dL	989 µmol/L
Glipizide (Glucotrol)	-	-	8 mg/dL	180 µmol/L
Ibuprofen (Motrin, Advil)	7 mg/dL	340 µmol/L	50 mg/dL	2425 µmol/L
Icodextrin	-	-	460 mg/dL	4600 mg/L
Levadopa	10 mg/dL	508 µmol/L	10 mg/dL	508 µmol/L
Methylhydroxyprogesterone	-	-	30 mg/dL	776 µmol/L
Metformin (Glucophage) Diabex)	-	-	50 mg/dL	3019 µmol/L
Methyldopa (Aldomet)	0.75 mg/dL	35.54 µmol/L	1.5 mg/dL	71 µmol/L
Nifedipine	-	-	18 mg/dL	520 µmol/L
Norethisterone	-	-	150 mg/dL	5026 µmol/L
Omeprazole (Prilosec)	-	-	8 mg/dL	232 µmol/L
Oxalic Acid	0.2 mg/dL	2 µmol/L	10 mg/dL	111 µmol/L
Quinine	1 mg/dL	31 µmol/L	2 mg/dL	62 µmol/L
Ranitidine (Zantac)	2 mg/dL	57 µmol/L	20 mg/dL	570 µmol/L
Salbutamol (Salbumol)	-	-	16 mg/dL	278 µmol/L
Salicylic Acid (Aspirin)	30 mg/dL	2170 µmol/L	60 mg/dL	4340 µmol/L
Simvastatin (Zocor)	-	-	8 mg/dL	191 µmol/L
Terfenadine	-	-	24 mg/dL	509 µmol/L
Tetracycline	0.5mg/dL	11.26 µmol/L	1.5 mg/dL	33.8 µmol/L
Thyroxine Sodium	5-12 mg/dL	65-155 µmol/L	40 mg/dL	516 µmol/L
Tolazamide (Tolinase)	5 mg/dL	160.8 µmol/L	15 mg/dL	482 µmol/L
Tolbutamide (Orinase)	24.03 mg/dL	890 µmol/L	64 mg/dL	237 µmmol/L
Warfarin (Coumadin)	1 mg/dL	32 µmol/L	10 mg/dL	324 µmol/L

*Substances in *italic* were tested with the new TrueMeasure test strip; other substances were tested with previous versions of the TrueMeasure technology test strip.

Table 7. Substances Tested for Interference with TrueMeasure Technology Test Strips (continued)*

Substance	Upper Limit of Therapeutic or Normal Concentration		Concentration Tested	
Endogenous				
Acetoacetate	1 mg/dL	0.1 mmol/L	20 mg/dL	2.0 mmol/L
Acetone	2.0 mg/dL	0.3 mmol/L	60 mg/dL	10.3 mmol/L
ß-hydroxybutyrate	6.3 mg/dL	0.5 mmol/L	264.6 mg/dL	21.0 mmol/L
Bicarbonate	29 mmol/L	29 mmol/L	30 mmol/L	30 mmol/L
Bilirubin, unconjugated	1.2 mg/dL	21 µmol/L	40 mg/dL	684 µmol/L
Cholesterol	300 mg/dL	7.77 mmol/L	500 mg/dL	12.95 mmol/L
Cholic Acid	1.5 µmol/L	1.5 µmol/L	6.0 µmol/L	6.0 µmol/L
Creatinine	1.5 mg/dL	133 µmol/L	4.5 mg/dL	397.8 µmol/L
Gamma Globulin	1.2 g/dL	12 g/L	1.68 g/dL	16.8 g/L
Glutathione	-	-	1.0 mg/dL	33 µmol/L
Hemoglobin	4 mg/dL	0.62 µmol/L	9 mg/dL	1.39 µmol/L
Lactic Acid	20 mg/dL	2.2 mmol/L	100 mg/dL	11.1 mmol/L
Pyruvic Acid	0.9 mg/dl	103 µmol/L	2.0 mg/dL	228 µmol/L
Triglycerides	190 mg/dL	2.15 mmol/L	1,500 mg/dL	16.95 mmol/L
Urea	38 mg/dL	13.6 mmol/L	500 mg/dL	178.5 mmol/L
Uric Acid	7 mg/dL	0.41 mmol/L	24 mg/dL	1.42 mmol/L
pH	7.35-7.45	7.35-7.45	7.25-7.66	7.25-7.66
Sugars				
Fructose	7.5 mg/dL	0.42 mmol/L	30 mg/dL	1.66 mmol/L
Galactose	20 mg/dL	1.11 mmol/L	60 mg/dL	3.33 mmol/L
Sucrose	-	-	50 mg/dL	1.46 mmol/L
Maltose	-	-	110 mg/dL	3.21 mmol/L
Xylose **			100 mg/dL	6.66 mmol/L
Anticoagulants				
Potassium EDTA	-	-	360 mg/dL	12.4 mmol/L
Lithium Heparin	-	-	5,600 U/dL	56,000 U/L

*Substances in *italic* were tested with the new TrueMeasure test strip; other substances were tested with previous versions of the TrueMeasure technology test strip.
**Do not use during Xylose absorption testing.

Effect of Sample Re-Application

In this study, an initial sample volume of 0.5 µL was followed by a second sample of 3.0 µL applied at two different time delays (2 and 5 seconds) at three different glucose concentrations (approximately 50, 90 and 350 mg/dL; 2.8, 5.0 and 19.4 mmol/L). The initial sample of 0.5 µL was insufficient to start the test. Comparable results were obtained from sample re-application compared to the control condition (a single 3.0 µL drop). Representative data are shown in Figure 3. The data indicates that if a test fails to start due to insufficient blood, a second drop of blood may be applied to the same test strip within 5 seconds of the first blood drop.

Effect of Sample Application Technique

Four different sample application methods were evaluated: hanging drop (control method), touching (lightly touching the finger to the test strip during blood application), smearing (smearing the finger lightly over the target area of the test strip during blood application) and end fill (applying the blood at the end of the test strip with the donor's palm up). There were no clinically significant differences between the three application methods and the control method. Representative data on the mean differences between methods are shown in Table 8.

Figure 3. Effect of Sample Re-application

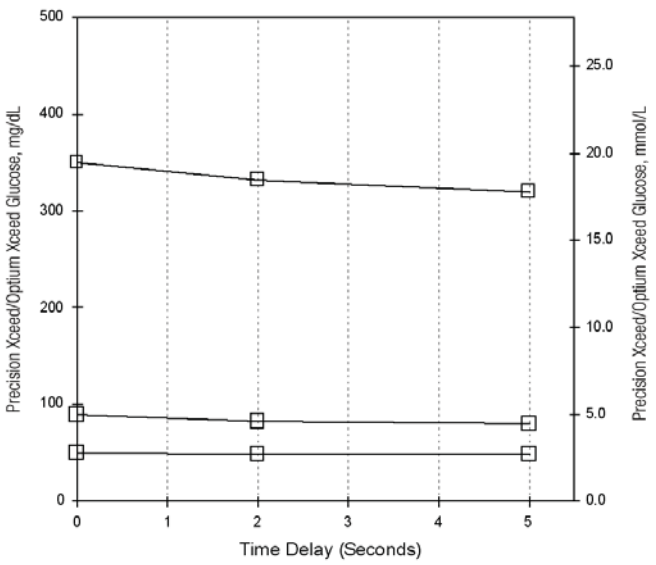


Table 8. Effect of Sample Application Techniques

Comparison	Difference in Mean % Bias
Hanging Drop* vs. Touching	0.2
Hanging Drop* vs. Smearing	-3.4
Hanging Drop* vs. End Fill	0.5

* Control method

Discussion

The new glucose test strip based on TrueMeasure technology showed excellent performance in this multicenter study:

Convenience and Ease-of-Use

The new TrueMeasure technology test strip is designed to be easy and convenient for frequent monitoring of blood glucose:

- **Speed:** It takes only 5 seconds per test.
- **Easier application of blood:** The user has multiple options and techniques available to apply blood. The user can apply blood to the top or the end of the test strip and the blood is automatically drawn into the reaction area. Its design provides equal convenience to left-handed and right-handed users. These features also make testing easier for caregivers or users with limited dexterity.
- **Requires less blood:** The new test strip requires 60% less blood than the previous TrueMeasure test strip. The small sample volume (0.6 µL) requirement facilitates alternative site testing.
- **No cleaning:** There is no test strip holder/guide or meter optics to clean.
- **Allows hand-held testing** in any position, enabling users to inconspicuously test anytime, anywhere. Some glucose meters are not designed for handheld testing. For example, one meter is required to be held at a certain angle when applying blood to the test strip and meter must not be positioned below the blood drop[2].
- **Allows re-application of sample:** If there is insufficient blood on the test strip to start a test, the user may add a second blood drop to the same test strip within 5 seconds of the first blood drop. It is not necessary to repeat the test with a new test strip. This may reduce the need to perform another finger-stick. With many glucose meters, adding a second blood drop can produce erroneous results[3,4,5].
- **Autostarts** when sample is detected
- **Easy-to-use:** The lay users in the user studies rated the new glucose test strip easy-to-use.

[2]Glucometer® DEX® Diabetes Care System User Guide, Bayer Corporation, 99B39529 Rev. 3/99, Page 6.
[3]One Touch® Ultra Test Strip insert, LifeScan, Inc. AW 060-181-05A 12/00.
[4]SureStep® Test Strips Insert, LifeScan, Inc., AW 052-549-01A, 1996.
[5]FastTake® Test Strip insert, LifeScan, Inc., AW 052-435-02A 3/99.

Reliable and Accurate Results for Home Monitoring

The new glucose test strip uses innovative technology, designed to maximize clinical accuracy in everyday testing for both fingertip and alternative site testing.

Reduced Analytical Error

The test strip is based on TrueMeasure technology with unique chemistry to increase performance. Accuracy was verified for capillary blood, across a haematocrit range of 30-55%, a linearity range of 20-500 mg/dL (1.1-27.8 mmol/L), and at high altitude (7,200 feet; 2,195 metres).

Reduced Use Error

Use error is a major concern in home monitoring of blood glucose. The new glucose test strip is designed to reduce use error in everyday testing conditions:

- Most glucose meters, including some newer models, produce erroneous results when a small drop of blood is used[6,7,8,9]. Erroneous results ranging from 85% lower to 39% higher were obtained in these studies when a small drop of blood was used. This is a common and significant error that users may not be aware of. The fill trigger electrode of the new test strip minimizes error from insufficient sample.
- Maintains accuracy when double-dosing (re-application with a second drop of blood)
- Maintains accuracy if the target area of the test strip is touched or the blood is smeared during sample application (reaction area is under a protective cover and adjacent to the sample application area).
- No timing error (no “off-meter dosing”, thus no user timing error).
- Biosensor technology is not affected by the ambient lighting conditions and there are no optical components to clean.
- TrueMeasure technology minimizes interference from medications and endogenous substances. By using a lower applied potential in the electrochemical reaction, the TrueMeasure test strip is not affected by high levels of reducing substances such as acetaminophen (paracetamol), uric acid or gentisic acid. Furthermore, other GDH-based test strips use the GDH-PQQ enzyme, which is less specific for glucose. Consequently, substances such as galactose (in newborns) and maltose (in dialysis patients that use icodextrin-containing solution for dialysis) can produce falsely elevated results[10,11]. The new test strip uses the GDH-NAD enzyme and is not affected by those substances.
- Each test strip is individually foil wrapped to protect it against moisture, which can deteriorate glucose test strips stored in vials that have not been capped promptly and tightly after each opening[12,13,14].

Cost Savings

The new test strip is designed with many strip-saving features:

- Double-dosing (applying a second drop of blood when the first drop is inadequate) minimizes the need to complete a test with another test strip.
- No meter optics means no wasted strips from invalid results due to bright light condition or a dirty optics.
- Individually foil wrapped test strips eliminate waste due to deterioration of test strips in vials not capped promptly and tightly after each opening.

[6]Haag BL, Leed LA. Susceptability of two home use glucose test strips to testing errors. *Diabetes*, 1999:48: A415.
[7]Velazquez, FR, Wright L, Ko K. Influence of glucose test strip design on the accuracy of test results. *Diabetes*, 1999:48: A349.
[8]Lewandrowski KB, Dan L. Effects of small sample volumes and interfering substances on two glucose meters. *Diabetes*, 1999:48: A387.
[9]Velazquez FR, Wright L, Herbert M, Wilson L. Effect of small sample volume, acetaminophen and uric acid on two glucose meters, *Diabetes*, 1998:47: A102.
[10]Oyibo SO, Pritchard GM, Mclay L, et al. Blood glucose estimation in diabetic patients on continuous ambulatory peritoneal dialysis for end-stage renal disease. *Diabetic Medicine* 2002;19:693-696.
[11]Riely SG, Chess J, Donovan KL, Williams JD. Spurious hyperglycaemia and icodextrin in peritoneal dialysis fluid. BMJ 2003; 327:608-609.
[12]Keffer P, Kampa IS. Instability of blood glucose test strips in uncapped vials. *Diabetes*, 1998:47: A170.
[13]Silverman BC, Humbertson SK, Stem JE, Nichols JH. Operational errors cause inaccurate glucose results. *Diabetes Care* 2000;23:429-430.
[14]Lilavivat U, Driggers D, Bocchicchia K, Okeke A. Erroneous diagnosis of diabetes mellitus from using improper storage of blood glucose test strips A case report with the study in the effect of exposed glucose test strips on erroneous self-monitoring of blood glucose (SMBG) results. *Diabetes* 2002;51:A481-48

In summary, the new test strip with TrueMeasure technology is uniquely designed to assure accuracy, reliability, ease of use, and cost savings for self-monitoring of blood glucose. Some of the key benefits provided by this new test strip are summarized in Table 9. Favorable responses from the lay users in this study confirm the advantages of the new test strip.

Table 9. Comparing Performance of Three Systems

Performance	Abbott TrueMeasure Test Strips	Accu-Chek™ Comfort Curve® Test Strips*	OneTouch® Ultra Test Strips*
Easy to use—sample can be applied on top or end of strip	**Yes**	No	No
Convenience (speed)— fast test time of 5 seconds or less	**Yes**	No	**Yes**
Convenience (small sample size)— less than 0.7 µL	**Yes**	No	No
Convenience—allows alternative site testing	**Yes**	No	**Yes**
Reduces cost (strip waste)—second drop of blood may be applied within 5 sec if first drop is too small to start test	**Yes**	**Yes**	No
Reduces medical errors—test designed not to start with inadequate blood sample	**Yes**	No	No
Reduces medical errors—test strips protected in individual foil packets	**Yes**	No	No
Reduces medical errors—results not affected by high levels of common medications or endogenous substances	**Yes**	No[1]	No[2]

*Trademarks are the property of their respective owners.

[1] Affected by high levels of acetaminophen (Tylenol), gentisic acid (from Aspirin), uric acid, bilirubin, galactose (in newborns), and maltose (from dialysis with icodextrin solution).
[2] Affected by high levels of acetaminophen (Tylenol), salicylates (Aspirin), ascorbic acid (vitamin C), and uric acid.

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