

October 2004



# EVALUATION

## MHRA 04116

### Bayer Ascensia Dex blood glucose meter



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# Bayer Ascensia Dex blood glucose meter

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## Summary

An evaluation has been performed on the Bayer Ascensia Dex blood glucose monitoring system with the Ascensia Autodisc blood glucose test sensors. The system is intended for home use by diabetics. It uses non-wipe biosensor technology for the measurement of glucose in capillary blood. Batch-specific calibration information is imprinted on the Autodisc, and obviates the operator having to input this information into the meter. The meter is simple to operate, is pre-calibrated and requires 2.5 to 3.5 µl of blood. The application of blood to the reaction area is simplified by the capillary fill system employed by the test sensor. Results are available in 30 seconds. The Dex gives whole blood-calibrated results.

The 108 Dex results, when compared with those obtained using either the hexokinase or the YSI 2300 method, gave a correlation coefficient of 0.99. There was a statistically significant negative average bias of -0.42 mmol/L against the hexokinase method and a statistically significant positive mean bias of 0.28 mmol/L against the YSI 2300. Results were on average 5.1 % lower than those obtained using the hexokinase method, with 25 % of results showing an absolute bias of more than 10 %, and 6 % of results showing a bias of more than 20 %. Against the YSI 2300 method, the mean percentage bias was approximately 2.5 %. Meter-to-meter variation in bias relative to the hexokinase method was not significant and the performances of the two Dex systems were similar. However, there was a batch-to-batch variation of approximately 0.4 mmol/L. Imprecision was found to be approximately consistent from one batch to another. Error grid analysis against the hexokinase method with meter B gave clinically acceptable results, whilst it just failed to give clinically acceptable results for meter A. No results fell in zones C - E. However, the YSI 2300 would classify both meters A and B as giving clinically acceptable results.

In the clinical study imprecision was estimated to be approximately 7 % on average across the concentration range studied when compared with the hexokinase results. In the laboratory study, imprecision (CV) of less than 5 % was attained at three out of the four concentrations (3.6, 9.3, 17.2, and 28.8 mmol/L). Total error of no more than 10 % was achieved at all four concentrations.

In the clinical study, there was evidence of haematocrit influence on the magnitude of the Dex bias at concentrations above 12 mmol/L. At concentrations of approximately 12 mmol/L a variation of around 5 mmol/L was found across a haematocrit range of 30 - 50 %. Equivalently, at concentrations of around 18 mmol/L and above a variation of approximately 11 mmol/L in the result from the Dex would be predicted.

## Introduction

Glucose estimations carried out using dry reagent strips or sensors, read visually or with a meter, may involve several operator dependent steps, increasing the possibility of error particularly when non-technical operators use the system. However, development in the manufacture of glucose test strips which use 'non-wipe' technology, reduction in the volume of blood required, (often by a "capillary fill" mechanism) and automatic timing sequences have helped in reducing the number of operator dependent steps. Issues related to the safety and management of point-of-care devices are covered in guidelines issued by the Medicines and Healthcare products Regulatory Agency (formerly the Medical Devices Agency)<sup>(1, 2)</sup>.

The Ascensia Dex glucose meter has been evaluated as part of an ongoing programme to assess the suitability of analytical systems for use in primary care and health screening locations. For information on other evaluation reports prepared by WASP see the MHRA website: [www.mhra.gov.uk](http://www.mhra.gov.uk).

## Instrument description

**Figure 1: Ascensia Dex blood glucose system**



The Ascensia Dex is a small, circular shaped, battery-powered meter for blood glucose estimations using non-wipe biosensor technology (figure 1). The Ascensia Autodisc test sensors are located within the meter as a foil covered disc containing ten sensors. Two-thirds down the front of the meter is a visual display panel covered by a blue pad, which can be moved left, forward or back allowing access to the meter's testing mode or the features

mode. To enter the test mode the blue pad is moved to the left and whilst holding it, the slide is moved forward all the way to push out a test strip and automatically turn on the meter. To turn the meter on in the 'features mode' the slide is moved forward to expose the visual display panel.

Below the visual display panel are two buttons marked A (moves to next setting) and B (changes the setting) used to: set time/date, set specific average times, reset meter options, review results, erase test results or transfer results to a computer. The 'end latch' at the top of the meter unclips to allow the test sensor disc to be inserted into the meter. The battery capsule is located on the side of the meter, and uses two 3-volt lithium button cell batteries (CR 2016).

**Figure 2: Test strip location**



Reagents are available in packs of five test sensor discs, each consisting of 10 test strips giving a total of 50 strips. The reagents are stored at room temperature, have a shelf life of up to 18 months, and can be used until the expiry date displayed on the disc. The temperature range for determination of glucose is 10 - 40 °C. The "end latch" at the top of the meter unclips to allow a test sensor disc to be inserted into the meter. The disc is inserted 'bumpy side up' by lining up the yellow arrow on the test strip disc with the

yellow line on the meter (figure 2). The disc is gently pressed into place under the two blue tabs (indicated by two blue arrows). Specifications of the Dex glucose system are given in table 1.

**Table 1: Details of the Ascensia Dex glucose system**

<b>Supplier</b>	Bayer plc Bayer House Strawberry Hill Newbury Berkshire RG14 1JA
<b>Reagent system</b>	Glucose oxidase / potassium ferricyanide mediator
<b>Measurement Principle</b>	chonoamperometric
<b>Calibration</b>	Automatic via code on AutoDisc
<b>Dimensions</b>	L 81 x W 66.2 x D 25.3 mm.
<b>Weight</b>	68 g (including batteries).
<b>Essential accessories</b>	Automatic lancing unit, lancet, absorbent tissue, batteries for the meter (Two 3-volt lithium batteries).
<b>Reagents</b>	Pack of 5 test sensor discs (x 50 sensors), quality control material.

## Operation of the meter

### Quality control

Aqueous, coloured quality control materials at three concentrations (low, normal and high) can be purchased from the manufacturer. The control materials are stored at temperatures between 15 - 30 °C, and have an open vial stability of six months from first use. The control ranges are lot specific for the test sensor in use, and the appropriate ranges for each control are printed on the sensors pack.

The meter is switched on by pushing the slide forward. For approximately one second a three character value 8.8.8 plus symbols of a drop, a battery and a tick, and another four-character value 88.88 appear on the visual display panel. The elements making up this number are checked to ensure that no part of it is missing (otherwise the meter may display incorrect results). The display first highlights the number (from 1 to 10) of sensors available for testing, alternating to displaying the last two glucose values with date and time stored in the meter's memory. If the meter has been opened since last use the programme number appears in the display. If there is no change, pressing button A will prompt the meter for blood application.

To perform a glucose measurement a test sensor is pushed out of the meter by sliding the blue pad and the slide to the left and forward. The meter cuts the foil

wrapping with a blade and pushes out a test sensor ready for use through a slot within the "end latch". Sample application is indicated by a symbol of a flasing drop appearing in the top left hand corner of the visual display panel. The manufacturer recommends that a drop of the control solution is squeezed out onto a clean surface, and the edge of the test sensor brought into contact with the control solution until the chamber is filled. The meter beeps, and begins a 30 seconds countdown for the measurement. At the end of the measurement procedure the results are displayed in mmol/L. The control results must be marked with a checkmark (✓) prior to storing the result in the meter's memory. This is accomplished by pressing button B twice. The used test sensor is ejected from the meter by closing the slide whilst pointing the meter down.

### **Fingerstick capillary blood glucose measurement**

Having analysed the quality control materials, the system is ready to measure a patient's glucose. Similar procedures are followed to those for the quality control measurement, by applying a drop of blood directly to the test sensor in place of the control solution.

Prior to performing a blood glucose measurement, and to reduce difficulties in obtaining a blood sample by improving circulation, the manufacturer recommends washing the hands with soap in warm water. A fingerstick sample of whole blood is obtained by lancing a finger. A small drop of blood is formed on the fingertip, and the front edge of the test sensor is brought into contact with the blood until the chamber is filled. The meter initiates the measurement automatically when the blood is detected in the test chamber, and begins a 30-second countdown. Results are automatically stored within the meter's memory when the slide is closed. A result can be deleted by pressing button B before closing the slide. Deleted results appear in the memory marked with a cross (X) and are deleted from the average of stored results. The meter switches itself off automatically after three minutes if left switched on or after 15 minutes if a test sensor has been loaded for a measurement.

The Dex has a memory capacity for 100 test results with a date/time stamp. The meter is capable of recalling the last result, all the results, or calculating the average over fourteen days. Pressing button M accesses the most recent blood test result . The down arrow allows the operator to scroll through all the stored data. The operator also has the option of deleting a blood test result so that it is excluded from the 14-day average. Deleted results appear in the memory marked with a cross "X".

The analytical range quoted by the manufacturer for the measurement of glucose concentration using the Dex is 0.6 to 33.3 mmol/L.

Coded error messages are shown on the visual display panel to indicate procedural or meter errors such as: battery dead, low battery, temperature outside the admissible range, the test strip removed during a test, defective test sensor disc, meter malfunction, meter switched on whilst the end catch is open, or operational

## Instrument description

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error. Glucose concentrations outside the limits of measurement are indicated by the messages 'HI' or 'LO'. The meter recognises temperatures outside the specified range of 10 to 40 °C as inadmissible; the result is marked with an "x" and will not be included in averages.

Complex maintenance is not required as the blood is applied to the test sensor externally to the body of the instrument and does not come into contact with the meter's internal components. However, minimal maintenance is required to ensure the meter and end catch are kept clean. The exterior and interior of the meter can be cleaned using a moist lint-free tissue with mild detergent or disinfecting solution, and dried using a lint-free tissue.

The Dex has additional features which allow the operator to log and assess the last two test results, the average over 14 days and four time specific average results for the 14 days testing period. Test results may be reviewed, erased or transferred to a personal computer.

## Methods and materials

The Ascensia Dex glucose meter has been evaluated as part of an ongoing programme to assess the suitability of analytical systems for use in primary care and health screening locations. The laboratory evaluation was carried out on instruments loaned by the manufacturer. The instruments were operated throughout according to the manufacturer's instructions. Reagents were obtained directly from the manufacturer.

The Dex system is calibrated to give whole blood results. It was tested in a clinical setting on 108 diabetic patients by obtaining capillary blood from a fingerstick. Accuracy and imprecision, meter-to-meter and strip batch-to-batch variation were assessed on two meters and two batches of test strips using conventional fingerstick capillary blood samples. Imprecision was assessed in separate laboratory experiments.

### Method comparison

#### Capillary blood

The performance of the glucose assay was evaluated by determining glucose concentration in capillary whole blood specimens from 108 patients. Results were compared with a routine laboratory method based on hexokinase/glucose-6-phosphate dehydrogenase following whole blood deproteinisation using perchloric acid and on a YSI 2300 analyser (Analytical Technologies, Farnborough, Hants).

To assess meter-to-meter and strip-to-strip variation, two Dex meters and two different batches of test strips were tested. Capillary blood specimens from a finger were obtained using the Safe-T-Pro lancet (Roche, UK) from patients attending the diabetic outpatient clinic or the Diabetes Centre at City Hospital, Birmingham. Samples were analysed immediately on two Dex meters following the manufacturer's instructions. A further 200 µl of blood from the same fingerstick was collected into a microvette tube (Sarstedt, Leicester, UK) containing lithium heparin as anticoagulant, and blood glucose estimation carried out immediately on the YSI 2300. Duplicate blood samples were also collected for the hexokinase assay. The influence of haematocrit on the glucose value obtained was assessed by carrying out haematocrit measurements on each patient sample in duplicate using a Microspin haematocrit centrifuge (Bayer Diagnostics, Newbury, UK).

#### Hexokinase assay

The blood sample for the hexokinase assay was collected into 40µl glass sodium heparin capillary tubes (Hirschmann Laborgerate GmbH, Eberstadt, Germany) in duplicate. The capillary tubes were then placed into two prefilled tubes containing 400 µl of 0.33M perchloric acid (Kabe Labortechnik, Nuembrecht-Elsenroth, Germany) and mixed vigorously for 10 seconds to allow protein precipitation. The perchloric acid tubes were centrifuged for five minutes at 10,000 rpm (Biofuge B, Heraeus Sepatech, Brentwood, Essex), and the precipitate decanted using a

positive displacement pipette. The samples were recentrifuged to ensure all traces of the precipitate were eliminated. The samples were stored overnight at -20 °C and analysed the following day on a BioStat BSD 570 using the BioStat Diagnostic System GLUC HK FS kit (Bio-Stat, Stockport, Cheshire).

### **YSI 2300**

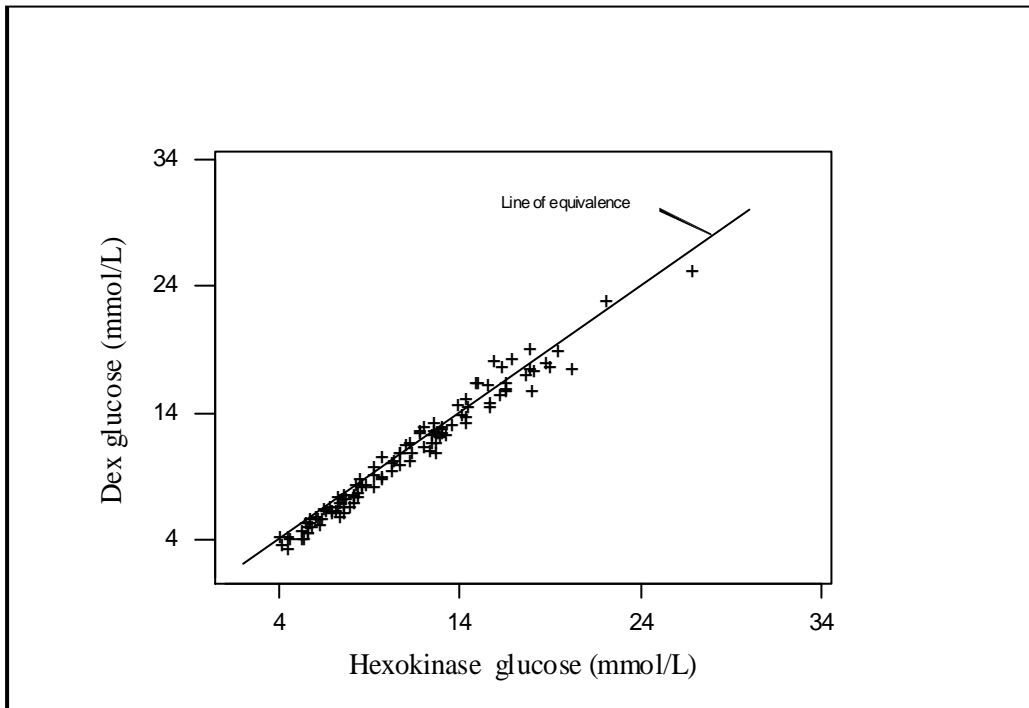
The YSI 2300 analyser uses a thin membrane containing immobilised glucose oxidase placed over a platinum anode. The glucose from the sample diffuses into the membrane, producing hydrogen peroxide, which is then oxidised at the platinum anode producing electrons. The electron flow is linearly proportional to the steady state hydrogen peroxide concentration, and therefore to the concentration of the glucose. The YSI 2300 was calibrated and maintained according to the manufacturer's instructions.

# Results

## Comparison with the hexokinase method

The correlation of the 108 results from patient specimens using the Dex meter and the hexokinase method is illustrated in figure 3 (correlation coefficient = 0.99). The line shown in figure 3 is the 45° line that would be seen if the Dex meter and the hexokinase gave identical results. Results were on average 5.1 % lower using the Dex meter than those obtained for the hexokinase method. Table 2 gives the mean glucose level obtained for the 108 patient specimens using the Dex meter and the hexokinase method. There is a statistically significant overall mean bias of -0.42 mmol/L, with standard error of 0.08 mmol/L ( $t_{107} = -5.40$ ,  $p < 0.001$ ).

**Figure 3: Correlation obtained for glucose results from 108 patients' fingerstick capillary blood samples using the Dex (meter A)**



**Table 2: Summary statistics of glucose results obtained by the Dex (meter A) and hexokinase method (n = 108)**

	Dex meter	Hexokinase	Dex - Hexokinase
<b>Mean</b> (mmol/L)	10.56	10.98	-0.42
<b>SD</b> (mmol/L)	4.71	4.57	0.79

Figure 4 shows the differences between the Dex meter and the hexokinase results plotted against the hexokinase result. Perfect agreement between the two sets of results would give a horizontal line of points passing through zero on the y axis and

## Results

a persistent trend away from that general pattern would indicate some pattern of bias. The pattern evident in figure 4 suggests negative bias at all concentrations but with imprecision increasing for concentrations above 10 mmol/L.

**Figure 4: Differences between the Dex (meter A) and the hexokinase results plotted against the hexokinase result**

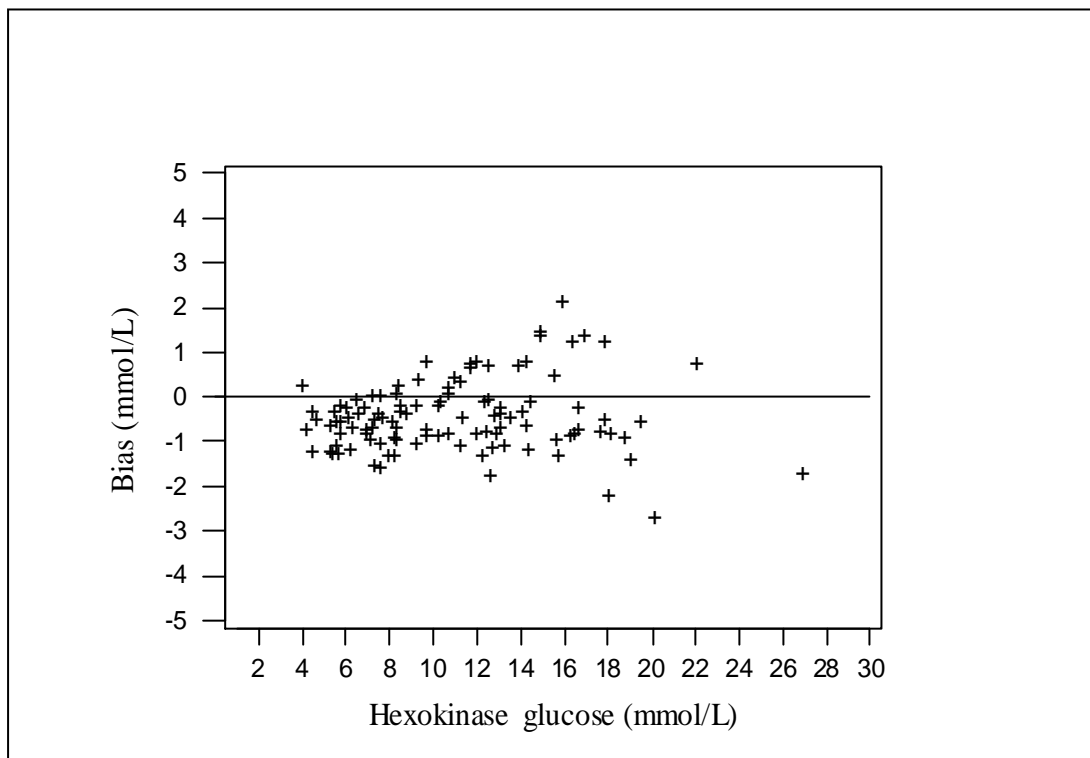
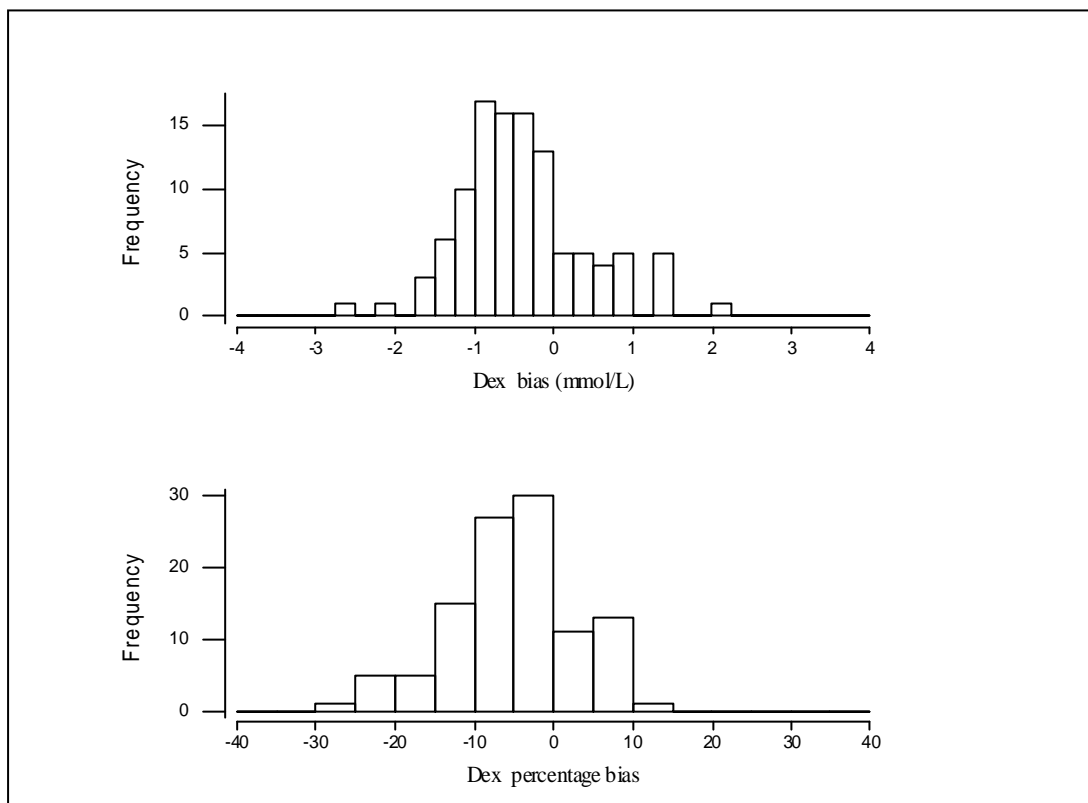


Figure 5 gives a histogram of the Dex meter bias, and confirms a negative overall bias. The corresponding plot of percentage bias shows 23 % of results from the Dex meter having a positive bias relative to the hexokinase method. There were 25 % of results with an absolute bias of more than 10 %, but 6 % results with an absolute bias of more than 20 %. A conventional regression analysis of Dex meter and hexokinase results (table 3) confirms the absence of a concentration dependent bias, which generally remains constant over the range of concentrations studied. The slope of 1.01 is not significantly different from unity.

## Results

**Figure 5: Histogram of the bias and percentage bias in results using the Dex (meter A)**



**Table 3: Regression statistics of the Dex (meter A) against the hexokinase glucose results**

	<b>Intercept (mmol/L)</b>	<b>Slope</b>
<b>Estimate (standard error)</b>	0.58 (0.20)	1.01 (0.02)
<b>95% confidence interval</b>	-0.18 to 0.98	0.97 to 1.05

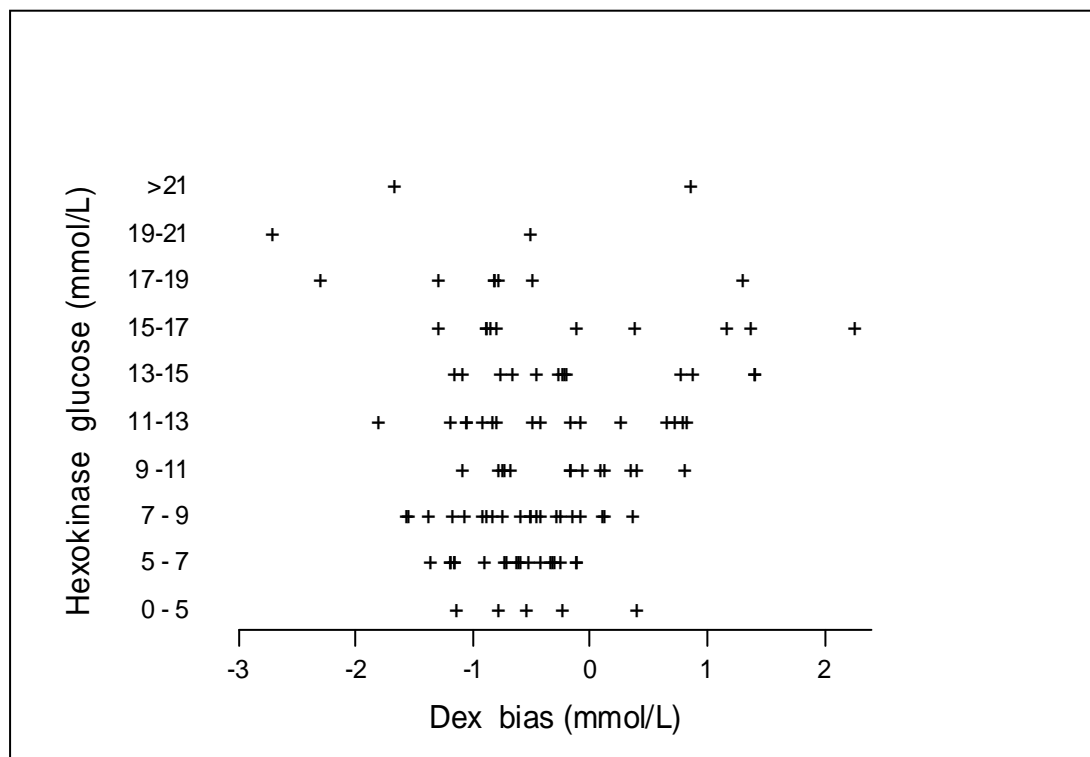
Dividing the data into groups according to the hexokinase result and calculating the bias of all Dex meter results relative to the hexokinase method gives the data shown in table 4. Figure 6 shows a corresponding group scatter plot of the Dex meter bias at each of the ten levels of hexokinase result used in table 4. The mean bias varies between 0.05 and -1.6 mmol/L or 0 and -11 % on average for most concentration levels for which a reasonable number of results were available, and the standard deviation of bias suggests imprecision of between 6 and 12 % on average. The about line standard deviation in the regression analysis reported in table 3, which should also provide an estimate of imprecision is 0.80 mmol/L or approximately 7 %. Both of these statistics are in broad agreement with standard deviations seen in table 4.

## Results

**Table 4: The mean bias of the Dex results (meter A) relative to the hexokinase results**

Hexokinase results (mmol/L)	Number of Results	Mean Dex bias mmol/L (% bias)	SD of bias mmol/L (% SD)
0 - 5	5	-0.48 (-11 %)	0.55 (12 %)
5 - 7	19	-0.65 (-11 %)	0.39 (7 %)
7 - 9	21	-0.61 (-8 %)	0.54 (7 %)
9 - 11	13	-0.20 (-2 %)	0.59 (6 %)
11 - 13	16	-0.33 (-3 %)	0.81 (7 %)
13 - 15	13	-0.04 (0 %)	0.86 (6 %)
15 - 17	10	0.05 (0 %)	1.20 (7 %)
17 - 19	7	-0.75 (-4 %)	1.05 (6 %)
19 - 21	2	-1.62 (-8 %)	1.52 (8 %)
>21	2	-0.48 (-2 %)	1.73 (7 %)

**Figure 6: Dex (meter A) biases relative to the hexokinase method at ten concentration levels as measured on the hexokinase method**



## Results

Figure 7a illustrates a significant negative correlation between the haematocrit and the bias in the Dex result ( $r = -0.36$ ,  $p < 0.001$ ). A linear regression analysis suggests a reduction of approximately 1.2 mmol/L in glucose concentration across the haematocrit range 30 to 50 %, the range of haematocrit studied.

**Figure 7a: Scatterplot of bias versus haematocrit for the Dex (meter A)**

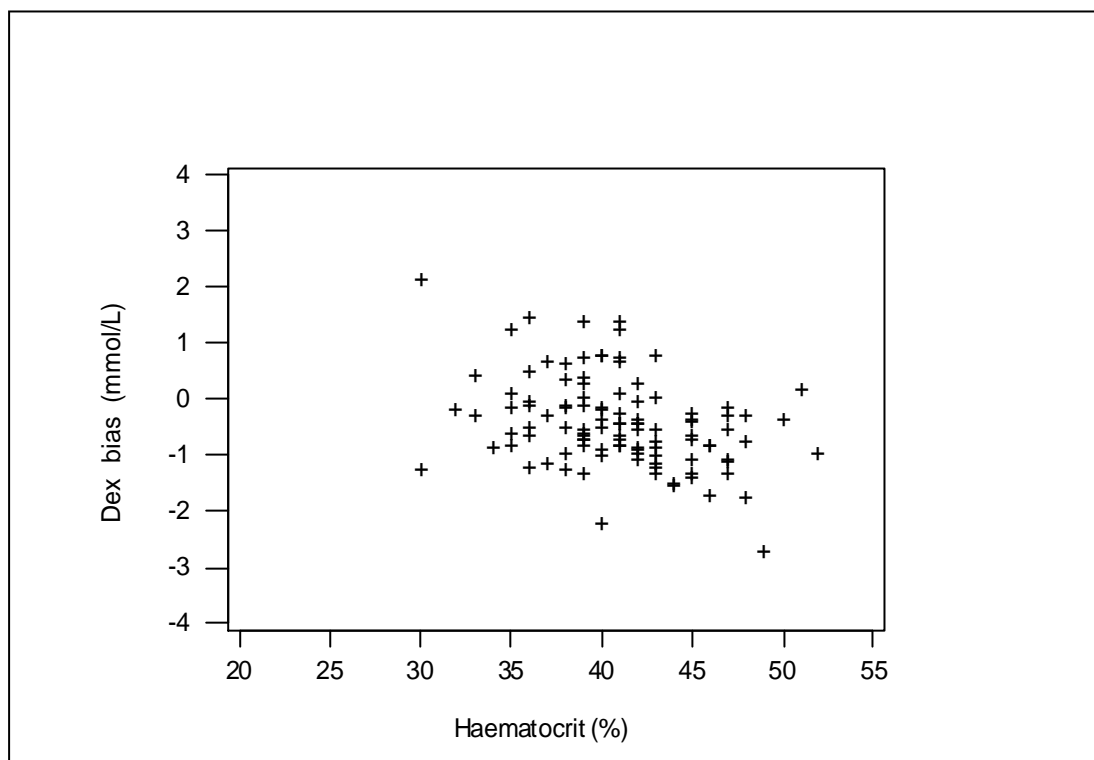
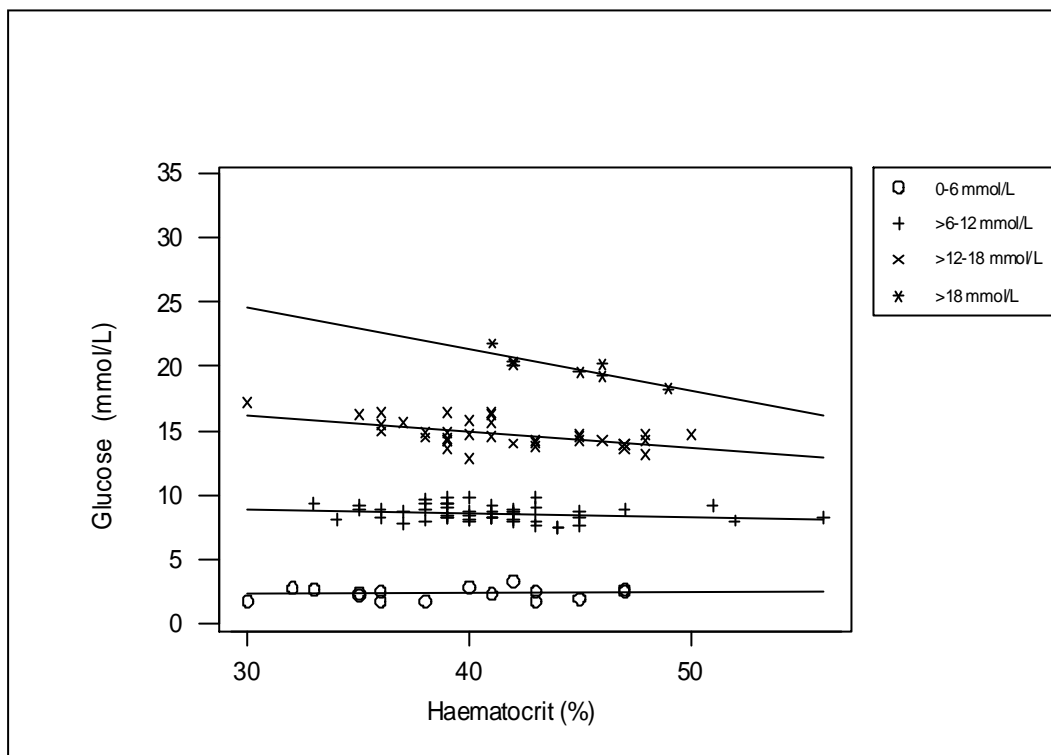


Figure 7b has been formed by calculating the bias of each Dex meter result and then displaying it at a level of 3, 9, 15 and 21 mmol/L depending on whether the corresponding hexokinase result fell in the intervals 0 to 6, > 6 to 12, > 12 to 18, or >18 mmol/L. This representation of bias at different concentration levels then gives an indication of how haematocrit has affected the accuracy of Dex results at different concentration levels. A significant effect of haematocrit would appear to occur at concentration levels above 12 mmol/L. This equates to an estimated reduction of 0.13 mmol/L per unit increase in haematocrit in the concentration range > 12 to 18 mmol/L and 0.32 mmol/L per unit increase in the concentration range > 18 mmol/L.

**Figure 7b: Bias versus haematocrit at four glucose concentrations for the Dex (meter A)**



## Comparison of two Dex meters

Two Dex systems designated meters A and B were used in parallel throughout the patient phase of this evaluation. In general, they gave similar performance, with the bias for meter B being almost identical at  $-0.41$  mmol/L with standard error 0.07. This bias is significantly different from zero,  $t_{107} = -5.63$ ,  $p < 0.001$ . The overall percentage biases from the two systems relative to the hexokinase method were  $-5\%$  for both meters A and B. Regression statistics for the Dex meter B were similar to those already reported for meter A. A similar table to table 4 for the second system suggests a mean bias varying from  $+0.2$  to  $-1.6$  mmol/L with varying concentrations. The mean difference overall between the two Dex systems was  $< 0.01$  mmol/L. Actual differences range from  $-2.1$  mmol/L to  $+1.4$  mmol/L.

An association between the bias on the Dex system and the haematocrit was also evident with meter B. For meter B the correlation between bias and haematocrit was  $r = -0.39$ ,  $p < 0.001$ .

## Comparison of two batches of test strips

Two batches of test strips were used during the patient stage of the evaluation: batch 1 lot number 1A2548AA; batch 2 lot number 1A2562AA. There was a significant difference in bias between the results from the two batches of test strips. The mean bias for the two batches of test strips was -0.60 mmol/L and -0.24 mmol/L ( $t_{106} = -2.42$ ,  $p = < 0.05$ ) using meter A, and -0.63 mmol/L and -0.21 mmol/L ( $t_{106} = -2.99$ ,  $p = < 0.01$ ) for meter B. Table 5 gives the mean bias and standard error of the mean for each batch of test strips using both meters. On both meters, batch 1 test strips gave a higher bias. However, there was no significant variation from meter to meter. For each meter and each batch the bias is significantly different from zero.

**Table 5: Mean bias using two Dex meters and two different batches of test strips**

	Number of results	Meter A mean bias (SEM)	Meter B mean bias (SEM)
<b>Batch 1 (lot 1A2548AA)</b>	53	-0.60 (0.10)	-0.63 (0.11)
<b>Batch 2 (lot 1A2562AA)</b>	55	-0.24 (0.11)	-0.21 (0.09)
<b>Note:</b> <b>SEM = standard error of the mean</b>			

Table 6 gives the standard deviation of the bias of results in each batch for each meter. These figures give some idea of the imprecision associated with each batch used with each meter and suggest that there is little variation in imprecision from batch to batch.

**Table 6: Standard deviation of bias using two Dex meters and two different batches of test strips**

	Meter A SD of bias (mmol/L)	Meter B SD of bias (mmol/L)
<b>Batch 1 (lot 1A2548AA)</b>	0.74	0.81
<b>Batch 2 (lot 1A2562AA)</b>	0.81	0.67

Table 7 gives regression statistics for each batch of test strips using meter A and hexokinase results, there is no significant difference in slopes between the two batches. Perfect agreement between hexokinase and the Dex would result in a slope of 1 and an intercept of 0. For both batches of test strips the slope is not significantly greater than unity, indicating no linear concentration dependent bias with test strips from these batches.

**Table 7: Regression statistics from two different batches of Dex test strips**

	Intercept (SE)	Slope (SE)
<b>Batch 1 (lot 1A2548AA)</b>	-0.67 (0.25)	1.01 (1.01)
<b>Batch 2 (lot 1A2562AA)</b>	-0.43 (0.30)	1.02 (0.02)

## Error grid analysis

Evaluations of devices for self-monitoring of blood glucose have been criticised for determining accuracy of the systems in ways which are not clinically useful<sup>(3-6)</sup>. Clarke et al<sup>(3)</sup> have developed an error grid analysis (figures 8a and 8b) of data to indicate if the results obtained by glucose systems used for self monitoring are clinically accurate and acceptable. This is based on trying to maintain a patient's glucose within the range 3.9 to 10.0 mmol/L, and the consequences of inappropriate treatment due to obtaining an incorrect result. Zone A represents glucose values which differ by < 20% from the reference. Zone B represents values that differ from the reference by >20%, but would lead to "benign or no treatment". Results in zone C would lead to "inappropriate intervention to alter an acceptable glucose concentration". Zone D depicts "dangerous failure to detect and treat errors", whilst zone E indicates an "erroneous treatment". The interpretation of error grid analysis has been extended<sup>(5)</sup> to specify that "an SMBG device can be considered acceptable if at least 95% of test results fall into the A zones and 0% fall in the C-E zones".

The results for the Ascensia Dex meters A and B are shown in Figures 8a and 8b. Using these criteria of Clarke et al on the 108 results from the Dex systems, 94 % of results from meter A and 97 % from meter B fell into zone A. The remaining results fell in zone B. Therefore the Dex meter B would be classified as giving clinically acceptable results, whilst meter A would be classified as giving unacceptable results. For meter A the six glucose results that fell in the B zone were all below 6 mmol/L, with an average discrepancy of 22.6 %, ranging from 20.5 to 26.7 % against the whole blood hexokinase reference method.

Figure 8a: Clinical evaluation of the Dex (meter A) by error grid analysis

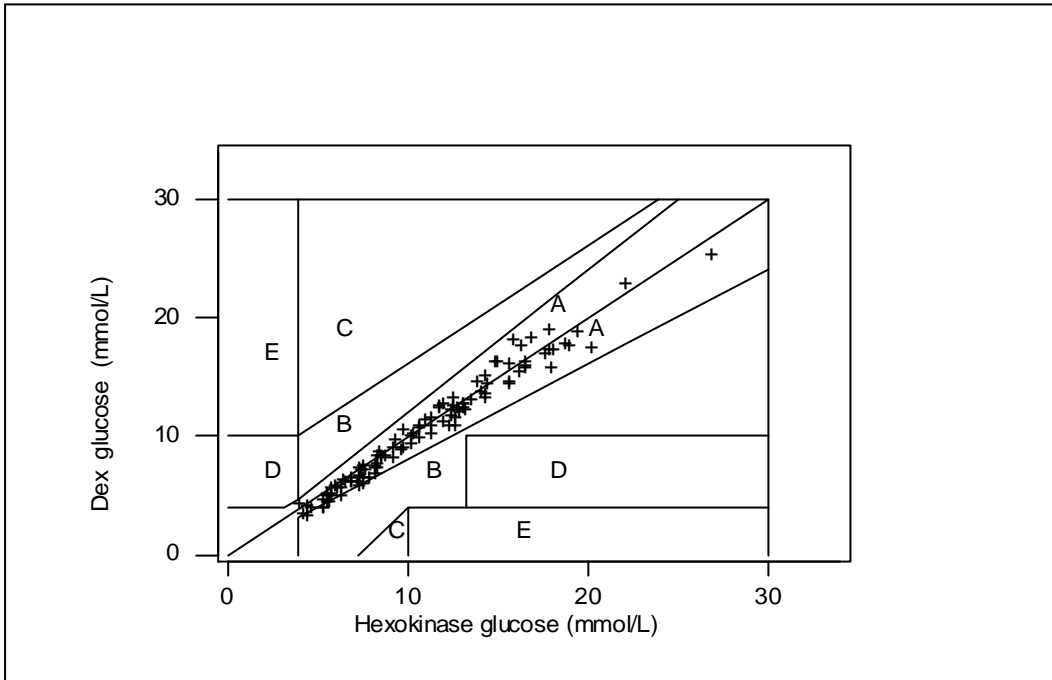
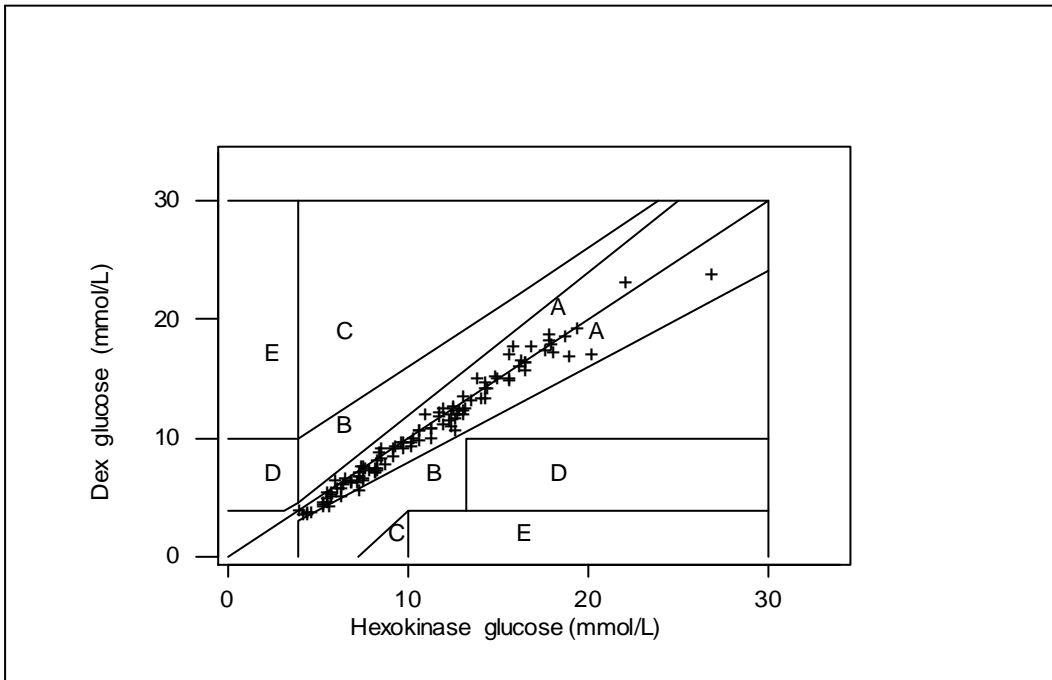


Figure 8b: Clinical evaluation of the Dex (meter B) by error grid analysis



**Notes:**

- Zone A - indicates clinically acceptable results
- Zone B - can lead to benign or no treatment
- Zone C - can lead to inappropriate intervention to alter an acceptable glucose concentration
- Zone D - dangerous failure to detect and treat
- Zone E - erroneous treatment

## Comparison with the YSI 2300

Correlation between 106 results from patient capillary specimens using the Dex meter and the YSI 2300 is 0.99. However, results were on average 2.5 % higher using the Dex meter than those obtained with the YSI 2300; figure 9 records the pattern of results produced by the two methods. Table 8 gives the mean glucose level obtained on the 106 patient specimens using the Dex meter and the YSI 2300. There is a significant positive overall mean bias of 0.28 mmol/L, with standard error of 0.74 mmol/L ( $t_{105} = 3.87$ ,  $p < 0.001$ ).

**Figure 9: Correlation obtained for glucose results from 106 patients' fingerstick capillary blood samples using the Dex (meter A) and YSI 2300**

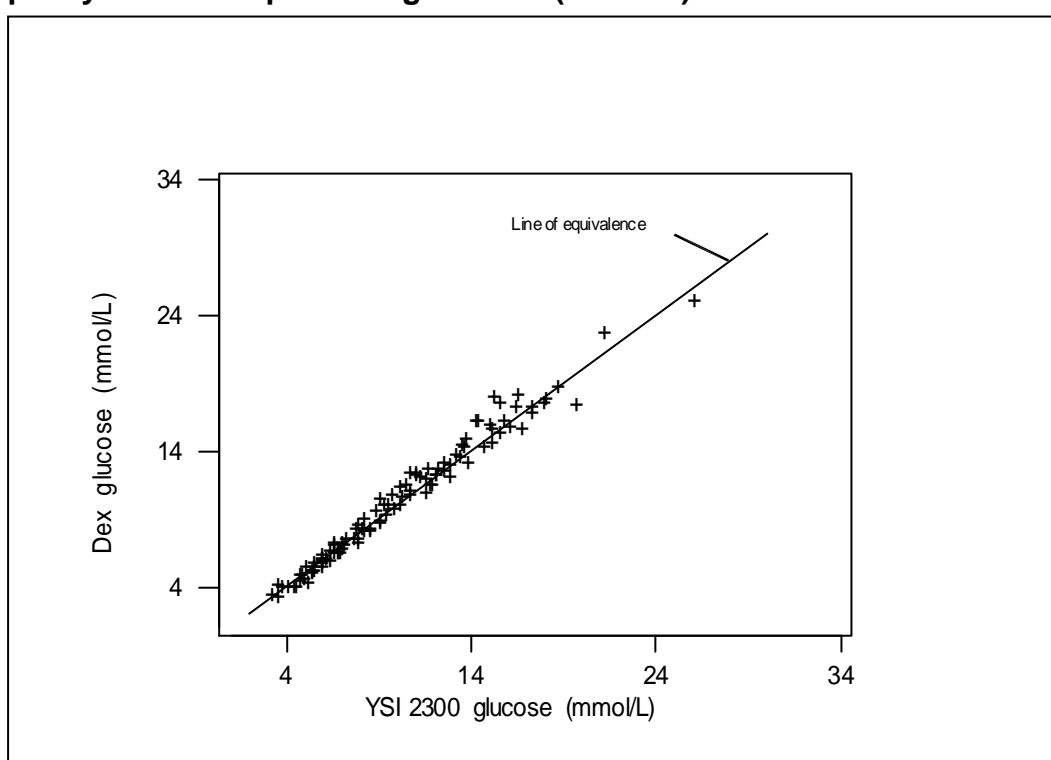


Table 9 shows regression statistics from a linear regression of Dex meter result on YSI 2300 result and gives evidence of a concentration dependent bias with the slope at 1.02, not significantly different from unity. However, it is evident from table 10, which gives the mean bias in the Dex meter relative to the YSI 2300 that there is variation in mean bias with concentration, but that variation is not linearly related to concentration. The bias becomes increasingly positive with increasing concentrations, but then sharply declines. One way ANOVA confirms the significance of the variation ( $F = 9.96$ ,  $p < 0.001$ ). As a percentage, the bias varies between -1 % and +6 % on average for most concentration levels for which a reasonable number of results were available. Correlation between bias and haematocrit is  $r = -0.31$  ( $p < 0.001$ ), slightly less pronounced than that seen when the hexokinase method was used as the reference.

## Results

**Table 8: Summary statistics for glucose results obtained by the Dex (meter A) and YSI 2300 (n = 106)**

	Dex meter	YSI 2300	Dex - YSI 2300
<b>Mean</b> (mmol/L)	10.48	10.20	0.28
<b>SD</b> (mmol/L)	4.70	4.52	0.18

**Table 9: Regression statistics of the Dex (meter A) against the YSI 2300 glucose results**

	Intercept (mmol/L)	Slope
<b>Estimate (Standard error)</b>	-0.07 (0.18)	1.02 (0.02)

**Table 10: The mean bias of the Dex (meter A) relative to the YSI 2300 glucose results**

YSI 2300 results (mmol/L)	Number of Results	Mean Dex meter bias mmol/L (% bias)
0 - 5	11	-0.02 (< 1 %)
5 - 7	24	0.02 (< 1 %)
7 - 9	13	0.17 (2 %)
9 - 11	16	0.64 (6 %)
11 - 13	14	0.31 (3 %)
13 - 15	10	0.82 (6 %)
15 - 17	10	0.67 (4%)
17 - 19	5	-0.18 (-1%)
19 - 21	1	-2.2 (-11%)
>21	2	0.35 (1 %)

In error grid analysis, 100 % of results fell within zone A for both meters A and B. Thus using the YSI 2300 as the reference method, the Dex meters would be classified as clinically acceptable with fingerstick capillary blood.

### Imprecision

The imprecision of the Dex system was determined on four meters at four different glucose concentrations. Blood was collected into lithium heparin vacutainer tubes (Becton Dickinson), and spiked with a 0.5 Molar glucose solution to the required glucose concentration. The spiked blood sample was allowed to equilibrate for 30 minutes at room temperature on a rotary mixer to a pO<sub>2</sub> equivalent to that of capillary blood, and aliquoted into 20 x 0.5 ml plastic tubes. An aliquot was selected randomly and used once only for glucose measurements on four Dex meters and the hexokinase method. Blood glucose measurements were also performed on the YSI 2300 throughout the experiment to ensure that the glucose level had not fallen due to glycolysis.

Twenty replicate glucose measurements were carried out at each level on the four meters using test strip lot number 1A2562AA. Results are summarised in Table 11. At glucose concentrations of 3.6, 9.3\*, 17.2\* and 28.8\* mmol/L (\* samples spiked with glucose), coefficients of variation (CVs) of 5.6, 3.6, 3.3 and 2.3 % were obtained respectively, relative to the hexokinase method. These CVs represent the variation between results performed on four randomly selected Dex meters. They do not include variations that might occur between batches of test strips. Total error (%), which includes imprecision and bias as outlined in table 11, was estimated at 6.6, 3.9, 9.8 and 2.3 % relative to the hexokinase reference results at the four concentration levels quoted. Relative to the YSI 2300 results the corresponding total error (%) was 6.5, 7.4, 10.6 and 9.5 % respectively.

The recommendations (7, 8) for extra-laboratory blood glucose analyses quote a total allowable error of no more than 10 % and an imprecision CV of no more than 5 %. The imprecision criterion was met at three of the four concentrations and the total error criterion was met at all four concentrations studied here. Against the YSI 2300 methodology the total error criterion was met at three of the four concentrations.

## Results

**Table 11: Imprecision of the Dex at four different glucose concentrations**

	Level 1	Level 2	Level 3	Level 4
<b>Hexokinase results</b> (mmol/L)	3.6	9.3	17.2	28.8
<b>Ascensia Dex</b>				
<b>Mean</b> (mmol/L)	3.7	9.5	18.8	28.7
<b>SD<sub>d</sub></b> (mmol/L)	0.20	0.31	0.59	0.66
<b>CV<sub>d</sub></b> (%)	5.6	3.3	3.3	2.3
<b>SD<sub>m</sub></b> (mmol/L)	NS	0.12	NS	NS
<b>CV<sub>t</sub></b> (%)	5.6	3.6	3.3	2.3
<b>Total error (%)</b> <b>(Hexokinase reference)</b>	6.6	3.9	9.8	2.3
<b>YSI 2300 results</b> (mmol/L)				
	3.6	8.9	17.1	26.3
<b>Total error (%) (YSI 2300 reference)</b>	6.5	7.4	10.6	9.5
<b>Notes:</b>				
SD <sub>d</sub> = replicate standard deviation (n = 20 on each of 4 meters)				
CV <sub>d</sub> = replicate coefficient of variation				
SD <sub>m</sub> = meter to meter standard deviation (4 meters)				
CV <sub>t</sub> = total (duplicate and meter) coefficient of variation				
Total variance = (SD <sub>d</sub> ) <sup>2</sup> + (SD <sub>m</sub> ) <sup>2</sup> + (bias) <sup>2</sup>				
Total error (%) = 100 x (total variance) <sup>1/2</sup> / mean reference glucose				
NS = Not significant				

## Operator dependency

Analytical systems for use by non-laboratory operators should have a minimal number of complex manoeuvres, to reduce the risk of obtaining incorrect results. The newer blood glucose systems have either reduced the number of complex manoeuvres or have integrated automated procedures to make the systems easier to use, thus reducing potential errors in glucose measurements. A major operator dependent step inherent to all analytical systems using capillary whole blood is in obtaining an adequate volume of free flowing blood. Introducing systems that require small sample volumes of 0.3 to 5 µl has reduced this potential error. The Ascensia Dex has also eliminated the need to manually input the calibration information (programme number) into the meter's memory as batch-specific calibration data for the test strips are printed on the Ascensia AutoDisc. The meter is automatically calibrated when the meter reads the information as the disc is advanced to the correct position.

A user-dependent step inherent to all systems is ensuring that the reagents are stored correctly following manufacturer's instructions and that they have not passed their expiry date.

Additional operator dependent steps identified for the Dex system were:

- performing the recommended maintenance procedures to ensure that the meter and test strip guide are kept clean
- ensuring that the control solution is tagged, so that the results are not included in calculation of averages.

## Instructions

Instructions for use of the meter included a 40-page fully illustrated user's manual. The instructions are concise and understandable for non-technical users. An instruction sheet is also provided in the reagent pack, and gives details for carrying out glucose measurements on the meter.

## Discussion and conclusions

The 108 Dex results, when compared with those obtained using either the hexokinase or the YSI 2300 method, gave a correlation coefficient of 0.99. There was an overall bias of -0.42 mmol/L relative to the hexokinase results, and 0.28 mmol/L relative to the YSI 2300 results. Relative to the hexokinase assay the bias remains relatively consistent as concentration increases, but relative to the YSI 2300 results reaches 0.8 mmol/L at the higher concentrations studied. There was significant batch-to-batch variation in mean bias of test strips for the Dex system. Meter-to-meter variation in bias was not significant and conclusions about the performance of the Dex system were on the whole consistent from one meter to the other. Error grid analysis relative to the hexokinase results would classify the system as clinically acceptable for meter B, with 97 % of the results falling in zone A. However, meter A gave 94 % of results in zone A, and therefore failed to meet the criterion of clinical acceptability. Zone B represents a 20 % difference in results, and in this case the six glucose results that fell in the B zone for meter A were all below 6 mmol/L, with an average discrepancy of 22.6 %. Relative to the YSI 2300 both meters A and B gave clinically acceptable results with 100 % of the results in zone A.

In the clinical study of fingerstick glucose measurements, imprecision was estimated to be approximately 7 % on average across the concentration range studied when compared with the hexokinase results. In the laboratory study, against the hexokinase method, imprecision (CV) of the results at glucose concentrations of 3.6, 9.3, 17.2 and 28.8 mmol/L was 5.6, 3.6, 3.3 and 2.3 % respectively, which meets the criterion for acceptable imprecision of no more than 5 % at three of the four concentration levels. The total error of 6.6, 3.9, 9.8 and 2.3 % respectively meets the criterion for acceptable total error of no more than 10 % at all levels against the hexokinase reference method (7, 8).

The manufacturer states that “at normal glucose levels, the Ascensia AutoDisc test strip results are not significantly affected by haematocrits in the range of 20 to 55 %. At glucose concentrations above 16.7 mmol/L, haematocrit levels above 55 % will cause lowered results, haematocrit levels below 25 % will cause high results.” From the clinical study, at glucose concentrations above 12 mmol/L, estimated variations of around 5 mmol/L would be expected across the haematocrit range 20 - 55 % in Dex result. Equivalently, at concentrations of around 18 mmol/L and above estimated variation of approximately 11 mmol/L in result from the Dex would be expected across the same haematocrit range. However, it should be emphasised that the entire haematocrit range of 20 - 55 % was not investigated in the clinical study and the figures for change over a haematocrit range of 20 - 55 % are only estimates based in the magnitude of change seen in the range 30 - 50 % encountered in this study.

In conclusion, the Dex system was easy to use gave results that were clinically acceptable against the YSI 2300 with both meters A and B. However against the hexokinase reference method, only meter B would be classified as giving clinically acceptable results. The use of non-wipe technology, no strip handling, automatic calibration, the ability to use as little as 2.5-3.5 µl of sample which is automatically drawn into the end of the test strip, and automatic timing sequence contributed to fewer operator dependent steps and the level of imprecision achieved.

## Acknowledgment

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# Appendix

## Manufacturer's comments

The following comments on this report have been received from Ms Melanie Collins, Manager Diabetes Support Group at Bayer Healthcare:

The Ascensia DEX was launched in the U.S. in 1997 at the same time that we in the U.K. launched the Ascensia Esprit. The Ascensia DEX is therefore a tried and tested blood glucose meter attaining high regard throughout the U.S. market.

Bayer HealthCare's commitment to providing quality products and services has prompted the inclusion of the Ascensia DEX into our European market. The autocalibration feature of this internal test sensor disc blood glucose monitoring system eliminates the need to 'code' the meter and thus reduces the potential for erroneous results.

Your evaluation has backed up our claims for imprecision, total error and clinical acceptability of the Ascensia DEX meter against the YSI.

I thank you for the completeness of this excellent study report and for providing the opportunity to comment.

## Procurement of blood glucose monitoring systems

Guidance for the procurement of blood glucose monitoring systems by NHS trusts has been developed by the NHS Purchasing and Supply Agency in co-operation with MHRA, UK suppliers and a Point of Care User Group. The NHS Purchasing and Supply Agency will work with trusts, providing both market and commercial advice for procurement projects. A procurement guide has been produced to allow maximum clinical and technical choice, whilst ensuring the business award is in accordance with EU procurement directives and represents value for money, a co-ordinated approach and best procurement practice for all stakeholders.

The guide comprises standard forms, standard terms and conditions, an outline specification, evaluation criteria and industry agreed tender documentation in a simple to use electronic format.

For further information on procurement guidance and support for point of care purchases please contact:

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NHS Purchasing and Supply Agency  
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Website Address:

<http://nww.pasa.nhs.uk/poct> (NHSnet users only)

<http://www.pasa.nhs.uk/dme>