Evaluation Report: Accu-Chek® Aviva Test Strips with Advanced Chemistry

Accu-Chek® Aviva test strips provide accurate and reliable blood glucose measurements.

SUMMARY

The Accu-Chek Aviva test strips with advanced chemistry have undergone a wide range of testing, including studies at 6 external sites and extensive internal testing. Test results demonstrate that the Accu-Chek Aviva system provides accurate and reliable blood glucose measurements under varied conditions, including the presence of maltose.

This document describes the Accu-Chek Aviva system and summarizes the test results for studies of accuracy, precision, hematocrit, and interfering substances.

Introduction

The Accu-Chek Aviva system serves as an accurate, reliable, and easy-to-use tool for monitoring blood glucose levels. The Accu-Chek Aviva meter and test strips with advanced chemistry provide people with diabetes with a reliable, 5-second test with proven sample sufficiency detection, wide hematocrit and environmental ranges, and a minimal sample volume of 0.6 µL.

The Accu-Chek Aviva system performs extensive quality checks with every test, enabling it to protect against factors such as temperature and hematocrit that can cause errors or inaccurate results in other systems. The system's advanced chemistry also provides accurate test results in the presence of maltose, making it suitable for use by:

- people receiving therapy with solutions containing maltose, which is present in some immunoglobulin preparations, and
- people on peritoneal dialysis using solutions containing icodextrin, such as EXTRANEAL™ dialysis solution.

Accu-Chek Aviva System Specifications

The table below indicates the specifications for the Accu-Chek Aviva meter and test strips with advanced chemistry.

Table 1. System Specifications

Category	Accu-Chek Aviva System Specification
Measurement principle	Mutant variant of quinoprotein glucose dehydrogenase (Mut. Q-GDH), electrochemical
Range of measurement	0.6 to 33.3 mmol/L
Measuring time	5 seconds
Operating temperature	8°C to 44°C (46°F to 111°F)
Operating humidity	10 to 90%
Sample volume	0.6 µL
Hematocrit range	10 to 65%
Altitude	Up to 3,094 meters (10,150 feet) above sea level
Sample types	Capillary, venous, arterial, neonatal
Test sites	Fingertip
Support and safety functions	• Automatic recognition and flagging of control solutions • Out-of-box date and time setting • Backup battery for date and time

Accu-Chek Aviva System Technology

With its patented technology, the Accu-Chek Aviva system gathers and analyzes extensive information to calculate a blood glucose measurement. Benefits of the technology include:

- ***Accurate and efficient temperature estimation.*** The Accu-Chek Aviva meter measures the temperature of the reaction zone on the test strip rather than relying on an internal thermistor. Therefore, the meter can accurately and efficiently compensate for temperature influences at the sample application site.
- ***Compensation for hematocrit effects.*** The Accu-Chek Aviva meter is able to compensate for hematocrit influences within a broad hematocrit range (10 to 65%).
- ***Sample sufficiency detection.*** Sample application is detected on one set of electrodes and adequate sample volume on another set. This feature helps prevent the user from underdosing a test strip and obtaining a potentially inaccurate result.
- ***Automatic recognition of Accu-Chek Aviva control solutions.*** The system can automatically distinguish quality control solutions from blood.
- ***Quality checks.*** The Accu-Chek Aviva meter conducts extensive quality checks with every test, including sample, strip, and system checks.

Meter Support and Safety Functions

- ***Out-of-box time and date setting.*** The Accu-Chek Aviva meter is shipped with the battery already inserted. The factory-set time and date can be confirmed with a simple button press, thereby minimizing meter setup time.
- ***Backup battery for time and date.*** A backup battery is housed in the meter to help preserve time and date information in the event that the main battery is no longer available. This feature ensures that the meter can provide accurate time stamps on results.

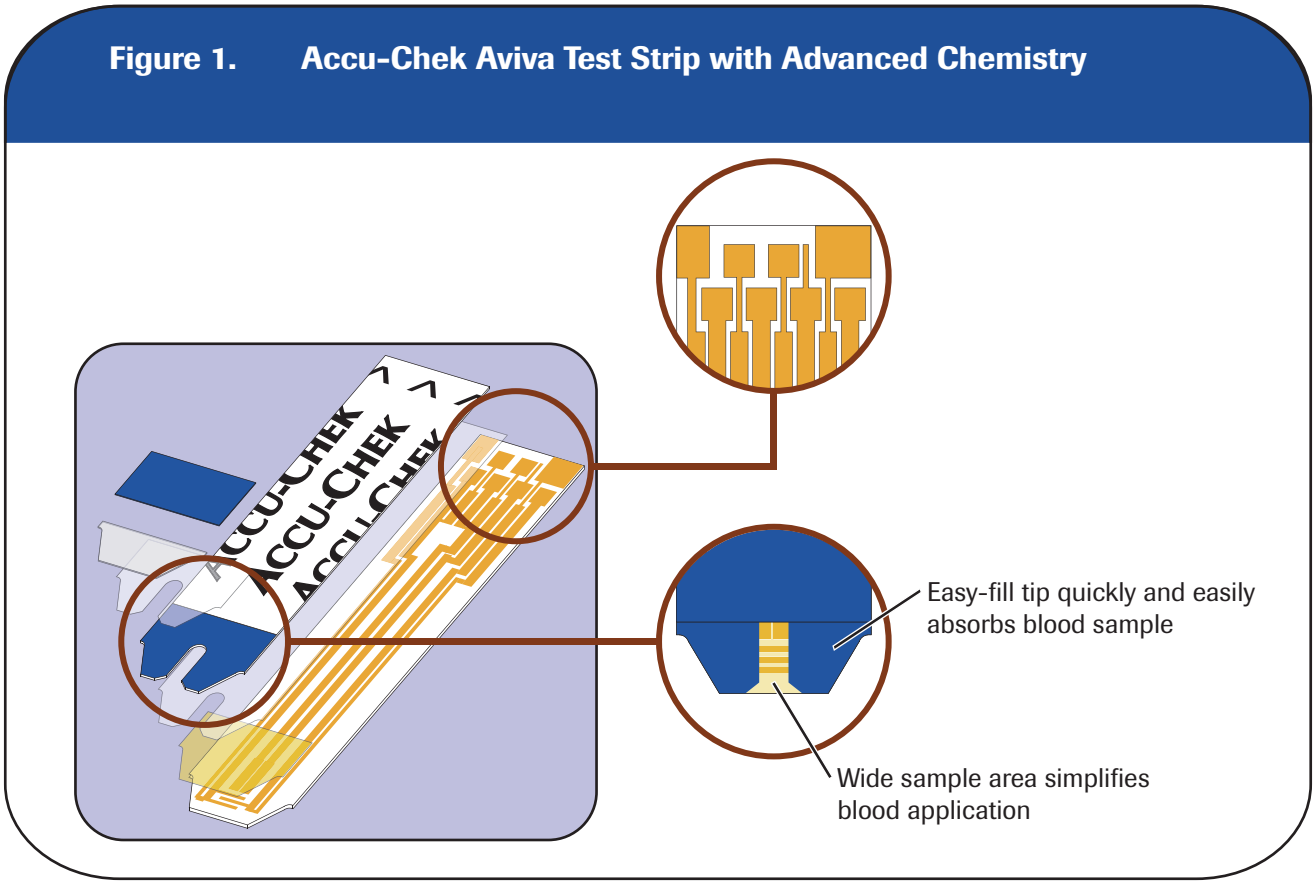
Accu-Chek Aviva Test Strip with Advanced Chemistry

Strip Architecture and Functionality

The Accu-Chek Aviva test strip with advanced chemistry contains eight gold electrodes (see Figure 1) that allow the system, along with its patented technology, to perform extensive quality checks. The following quality checks ensure that the user obtains an accurate result:

- ***Sample checks***
  - Verify whether the correct amount of blood is applied
  - Detect and identify the sample as blood or a control solution
- ***System checks***
  - Detect humidity exposure
  - Detect variations in temperature
- ***Strip checks***
  - Evaluate the test strips and reagent for potential damage or abuse, including:
    - exposure to high humidity
    - scratches on the strip electrodes

Figure 1. Accu-Chek Aviva Test Strip with Advanced Chemistry



Strip Reaction Principle

The enzyme on the Accu-Chek Aviva test strip with advanced chemistry, Mut. Q-GDH from Acinetobacter calcoaceticus, recombinant in E. coli, converts the glucose in the blood sample to gluconolactone. This reaction creates a harmless DC electrical current that the meter interprets for blood glucose. The sample and environmental conditions are also evaluated using a small AC signal.

Accuracy Studies Using the Accu-Chek Aviva System

Accuracy with Capillary Whole Blood

A study was conducted to assess the accuracy of the Accu-Chek Aviva system with capillary blood samples. Technicians at a participating facility performed capillary finger sticks on 100 patients. Two glucose test strips from three individual strip lots were dosed for each patient, for a total of 200 glucose meter results per lot. These results were compared to whole blood reference samples, which were analyzed on a Cobas c501 analyzer using glucose hexokinase methodology and mathematically converted to IFCC plasma-like reference values. The glucose reference values ranged from 1.9 to 25.2 mmol/L, and the hematocrit range tested was 34 to 52%.

Results of the study were assessed per the following acceptance criteria:

- 95% of the individual glucose results shall fall within ±0.83 mmol/L of the reference results at glucose concentrations less than 5.6 mmol/L and within ±15% at glucose concentrations greater than or equal to 5.6 mmol/L.

Each of the lots tested met the acceptance criteria. The data for one representative strip lot are presented in Figure 2 as a bias plot and summarized in Table 2. As seen in Figure 2 and Table 2, 100% of the data were within these bias requirements and the acceptance criteria were clearly met. These data indicate that the Accu-Chek Aviva system provides accurate results with capillary blood samples.

Figure 2. Accuracy with Capillary Whole Blood

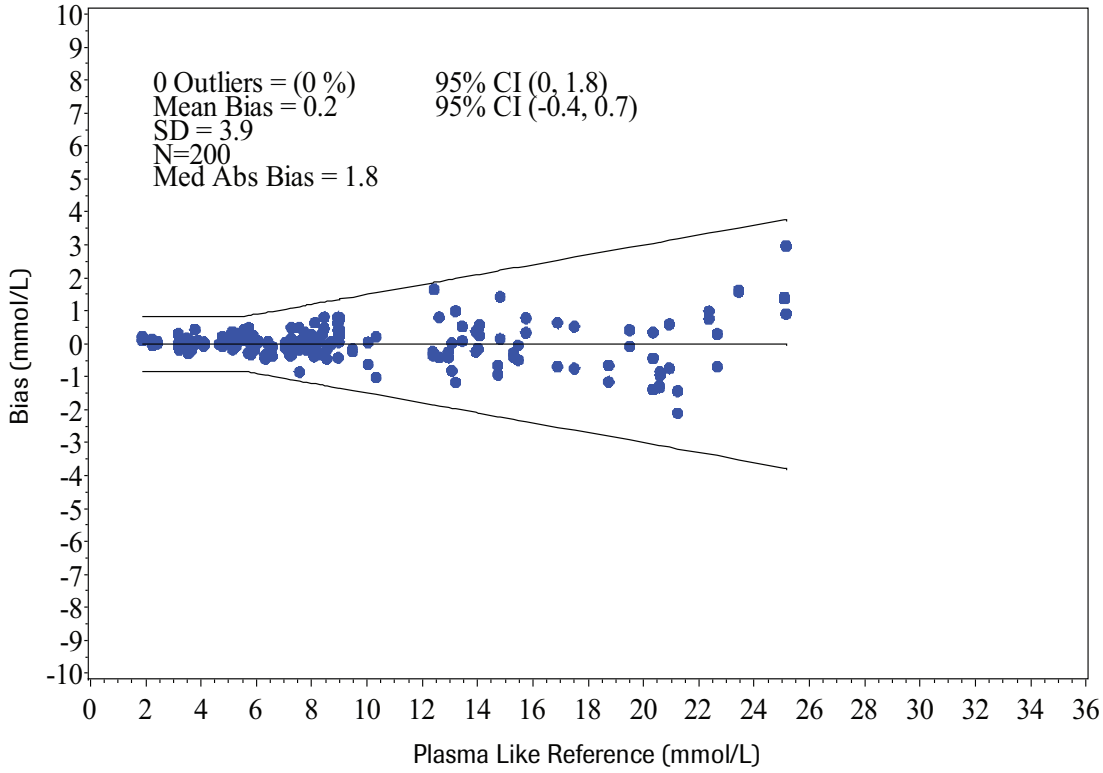


Table 2. Accuracy with Capillary Whole Blood

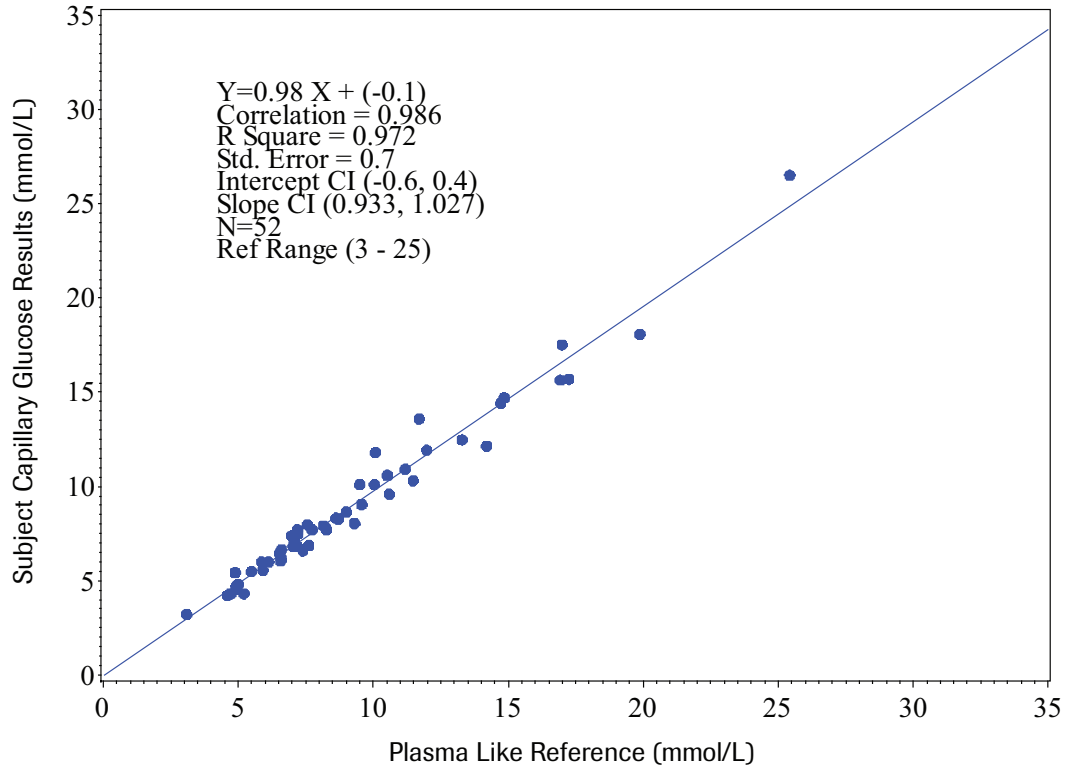
	Within ±0.28 mmol/L	Within ±0.55 mmol/L	Within ±0.83 mmol/L
Results <5.6 mmol/L	53/58 (91.4%)	58/58 (100%)	58/58 (100%)
	Within ±5%	**Within ±10%**	**Within ±15%**
Results ≥5.6 mmol/L	103/142 (72.5%)	139/142 (97.9%)	142/142 (100%)

Accuracy with Capillary Whole Blood Performed by Patients

Patients at one facility were asked to read the labeling provided with the Accu-Chek Aviva system, and to subsequently perform a finger stick and dose a test strip from one of three independent strip lots. The patients were given no instruction by a trained technician. The patient results were compared to whole blood reference samples, which were analyzed on a Roche/Hitachi 917 analyzer using glucose hexokinase methodology and mathematically converted to IFCC plasma-like reference values. Data from 163 patients were used in the analysis. The glucose reference values ranged from 2.7 to 25.4 mmol/L, and the hematocrit range tested was 27 to 53%.

The results for one representative strip lot, analyzed by linear regression, are presented in Figure 3. For this strip lot, data from 52 patients were used in the analysis and the glucose reference values ranged from 3.1 to 25.4 mmol/L. The graph shows strong correlation between the patient finger stick results and the reference method (0.986), indicating minimal scatter around the regression line. These data demonstrate that the untrained user can obtain accurate results with capillary blood.

Figure 3. Accuracy with Capillary Whole Blood – Performed by Patients

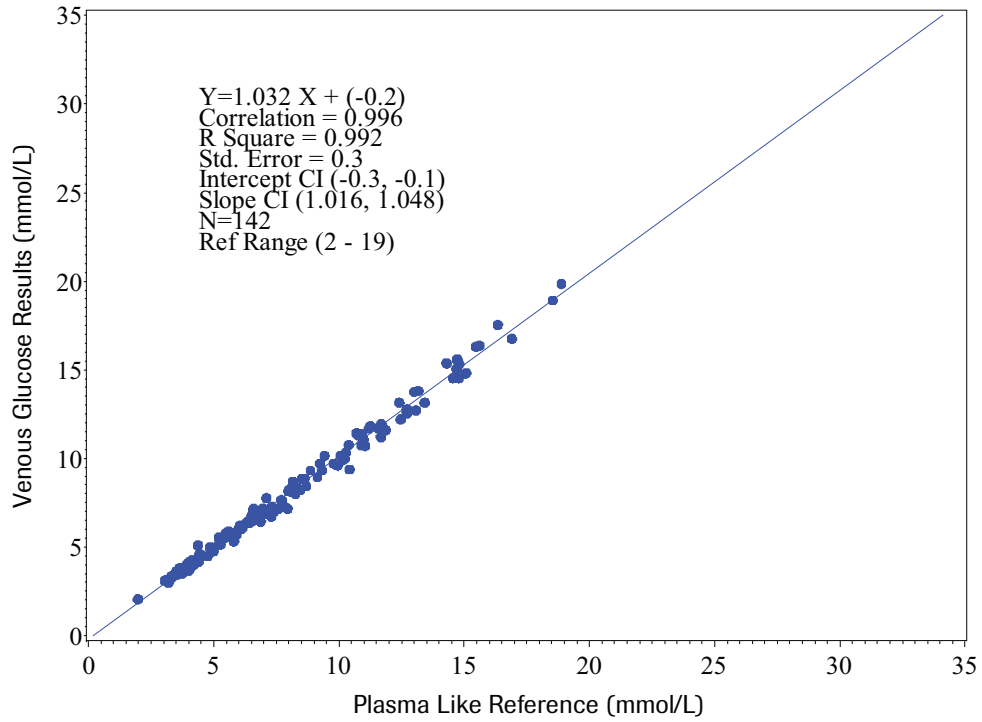


Accuracy with Venous Whole Blood

Technicians at one clinical site collected blood via venipuncture. Test strips from three independent lots were then dosed with the venous blood samples by the technicians. These results were compared to whole blood reference samples, which were analyzed on a Roche/Hitachi 917 analyzer using glucose hexokinase methodology and mathematically converted to IFCC plasma-like reference values. Data from 142 patients were used in the analysis. The glucose reference values ranged from 2.0 to 18.9 mmol/L, and the hematocrit range tested was 28 to 58%.

The results for one representative strip lot, analyzed by linear regression, are presented in Figure 4. The graph illustrates good correlation to the reference method (0.996) and a small standard error (0.3), indicating minimal scatter around the regression line. These data confirm that the Accu-Chek Aviva system provides accurate results with venous blood samples.

Figure 4. Accuracy with Venous Whole Blood



Accuracy with Neonatal Capillary Whole Blood

Studies were conducted to assess the accuracy of the Accu-Chek Aviva system with neonatal capillary blood samples. Technicians at a participating facility performed capillary heelsticks on newborns (less than 30 days old) and dosed test strips from three independent strip lots. These results were compared to whole blood reference samples, which were analyzed on a Roche/Hitachi 917 analyzer using glucose hexokinase methodology and mathematically converted to IFCC plasma-like reference values. Data from 92 patients were used in the analysis, and the glucose reference values ranged from 1.2 to 5.2 mmol/L.

The results for one representative strip lot, analyzed by linear regression, are presented in Figure 5. The graph shows good correlation to the reference method (0.987), and a very small standard error (0.1), indicating minimal scatter around the regression line. These data indicate that the Accu-Chek Aviva system provides accurate results with neonatal whole blood samples.

To further demonstrate accuracy with capillary neonate blood at glucose concentrations less than 2.8 mmol/L, additional analysis was performed on three independent strip lots using heel stick blood samples from 35 neonates. Table 3 shows the pooled bias of the individual capillary heelstick samples with a glucose concentration less than 2.8 mmol/L. As shown, the Accu-Chek Aviva system provides accurate results with neonatal whole blood samples at glucose levels less than 2.8 mmol/L.

Figure 5. Accuracy with Neonatal Capillary Whole Blood

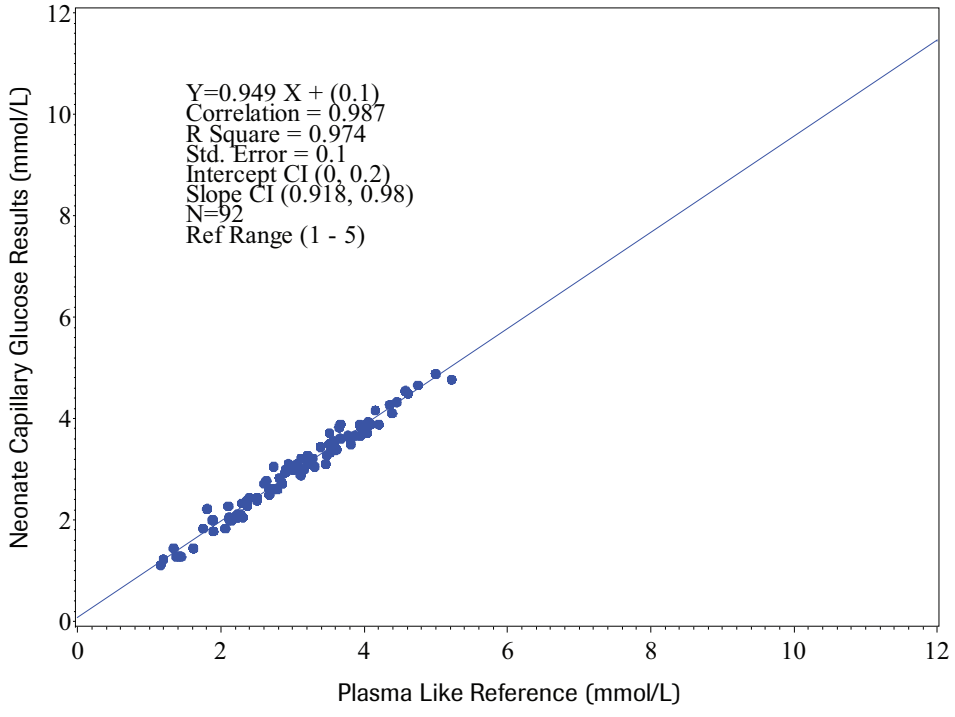


Table 3. Pooled Lot Bias for Neonate Capillary Samples Under 2.8 mmol/L Glucose

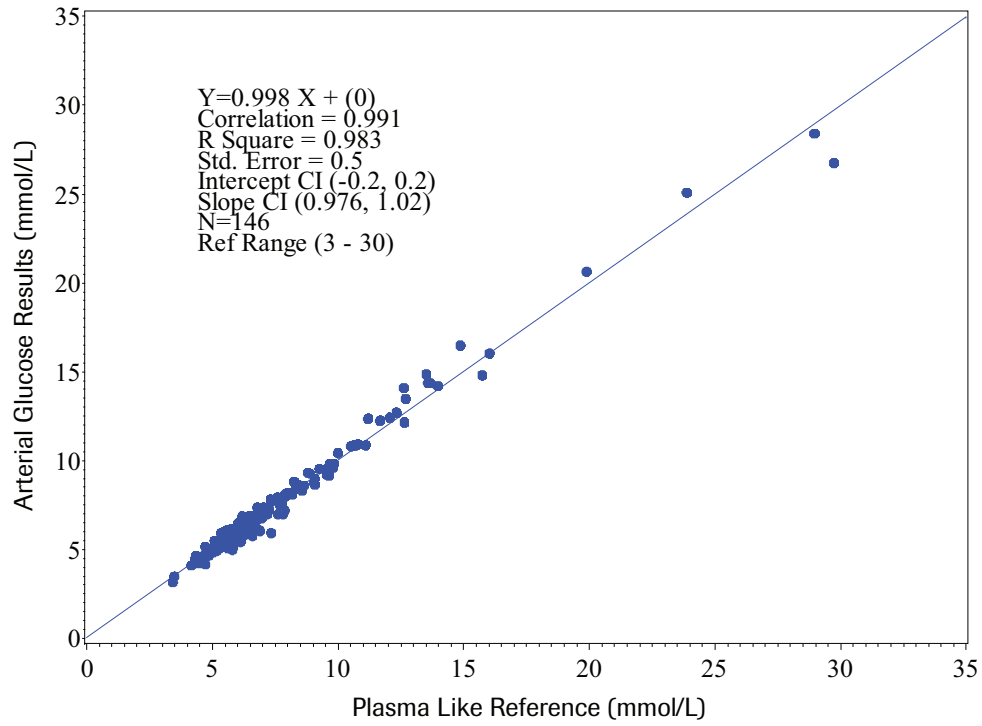
	N	Mean Bias (mmol/L)
Results <2.8 mmol/L	103	-0.07

Accuracy with Arterial Whole Blood

Technicians at one clinical site collected arterial blood using their standard operating procedure. Test strips from three independent lots were then dosed with the arterial blood samples by the technicians. These results were compared to whole blood reference samples, which were analyzed on a Roche/Hitachi 917 analyzer using glucose hexokinase methodology and mathematically converted to IFCC plasma-like reference values. Data from 146 patients were used in the analysis. The glucose reference values ranged from 3.4 to 29.7 mmol/L and the hematocrit range tested was 24 to 55%.

The results for one representative strip lot, analyzed by linear regression, are presented in Figure 6. The graph illustrates good correlation to the reference method (0.991) and a standard error of 0.5, indicating minimal scatter around the regression line. As shown, the Accu-Chek Aviva system provides accurate results with arterial blood samples.

Figure 6. Accuracy with Arterial Whole Blood



Accuracy at Elevated Altitude

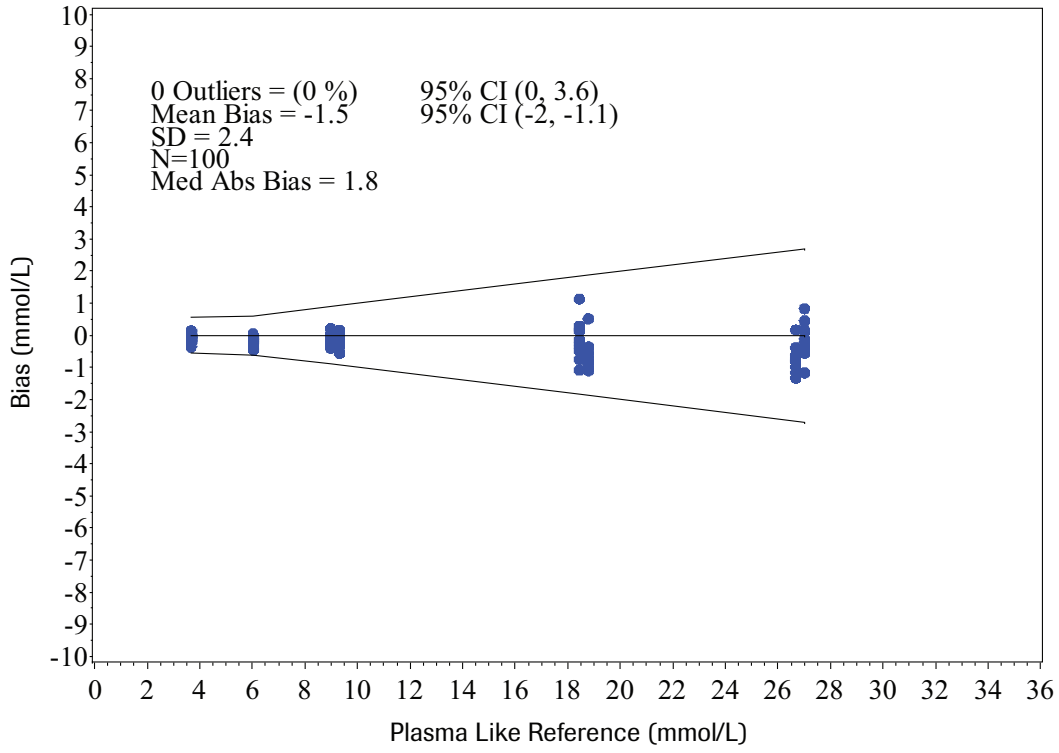
Testing occurred under simulated conditions at 3,094 meters (10,150 feet) above sea level in a hypobaric chamber. Venous whole blood was collected from one donor and spiked with glucose solution to obtain varying glucose concentrations. Five levels of glucose concentrations were tested on two strip lots inside and outside of the chamber. The pooled blood hematocrit result was 47%.

In Figure 7, the data for the two strip lots are presented in a bias plot and assessed per the following acceptance criteria:

- 80% of the individual glucose results shall fall within ±0.55 mmol/L of the reference results at glucose concentrations less than 5.6 mmol/L and within ±10% at glucose concentrations greater than or equal to 5.6 mmol/L (shown in Figure 7).
- 95% of the individual glucose results shall fall within ±0.83 mmol/L of the reference results at glucose concentrations less than 5.6 mmol/L and within ±15% at glucose concentrations greater than or equal to 5.6 mmol/L.

As seen in Figure 7, 100% of the data were within these bias requirements and the acceptance criteria were clearly met. These data indicate that the Accu-Chek Aviva system provides accurate results at elevated altitude.

Figure 7. Accuracy at Elevated Altitude



Accu-Chek Aviva System Precision

The precision of the Accu-Chek Aviva system was assessed using both aqueous control solutions and venous blood samples. For aqueous control solutions, thirty vials of test strips from each of three lots were allocated per sample type and level. For venous blood samples, fifty vials of test strips from each of three lots were allocated per sample type and level. Ten replicates per vial were collected and the overall SD or CV was calculated (based on glucose level).

The following control levels were used in the precision studies:

- **Low:** 1.7 to 3.3 mmol/L
- **Mid:** 5.4 to 7.3 mmol/L
- **High:** 14.1 to 19.1 mmol/L

The following spiked venous blood levels were used in the precision studies:

- **1:** 1.7 to 2.8 mmol/L
- **2:** 2.8 to 6.1 mmol/L
- **3:** 6.2 to 8.3 mmol/L
- **4:** 8.4 to 13.9 mmol/L
- **5:** 13.9 to 22.2 mmol/L

Table 4 and Table 5 show the results of the precision testing with controls and blood, respectively. Acceptable performance is defined as:

- At glucose concentrations less than or equal to 4.2 mmol/L, a standard deviation (SD) of less than or equal to 0.28 mmol/L
- At glucose concentrations greater than 4.2 mmol/L, a coefficient of variance (CV) less than or equal to 5%.

Results show that all precision estimates for control and spiked venous blood are below the 0.28 mmol/L or 5% threshold. In fact, all SD values for control solutions and venous blood at glucose levels 4.2 mmol/L and below are at or below 0.07 mmol/L, while all CV values for control solutions and venous blood at glucose levels over 4.2 mmol/L are at or below 2.5%. These data indicate that the Accu-Chek Aviva system provides precise results with both control solutions and whole blood.

Table 4. System Precision (Day-to-Day) – Control Solutions

	Low	Mid	High
N	10	10	10
Mean (mmol/L)	2.5	6.5	16.6
SD (mmol/L)	0.04	–	–
CV (%)	–	1.3	1.3

Table 5. System Precision (Within-Run) – Blood

	1	2	3	4	5
N	10	10	10	10	10
Mean (mmol/L)	2.0	4.3	7.0	11.1	18.3
SD (mmol/L)	0.07	0.1	0.1	0.3	0.3
CV (%)	–	2.5	2.0	2.3	1.8

Impact of Hematocrit

Five levels of glycolized venous blood with the target glucose level at 2.2, 3.6, 6.7, 19.4, and 27.7 mmol/L were tested with hematocrit levels adjusted to 10, 15, 20, 25, 30, 50, 55, 60, and 65% to determine the impact of hematocrit on the performance of the Accu-Chek Aviva system. These results were compared to a sample at nominal hematocrit (43%).

Three Accu-Chek Aviva strip lots were tested and all lots met the following acceptance criteria:

- For glucose concentrations less than 5.6 mmol/L, a mean bias of less than or equal to 0.55 mmol/L
- For glucose concentrations greater than or equal to 5.6 mmol/L, a mean bias less than or equal to 10%.

The results for one representative lot are shown in Figure 8 and Figure 9 (at low glucose concentrations and mid and high glucose concentrations, respectively). Data from all three lots confirm that the Accu-Chek Aviva system supports a claimed hematocrit range of 10 to 65%.

Figure 8. Impact of Hematocrit — Low Glucose Concentrations

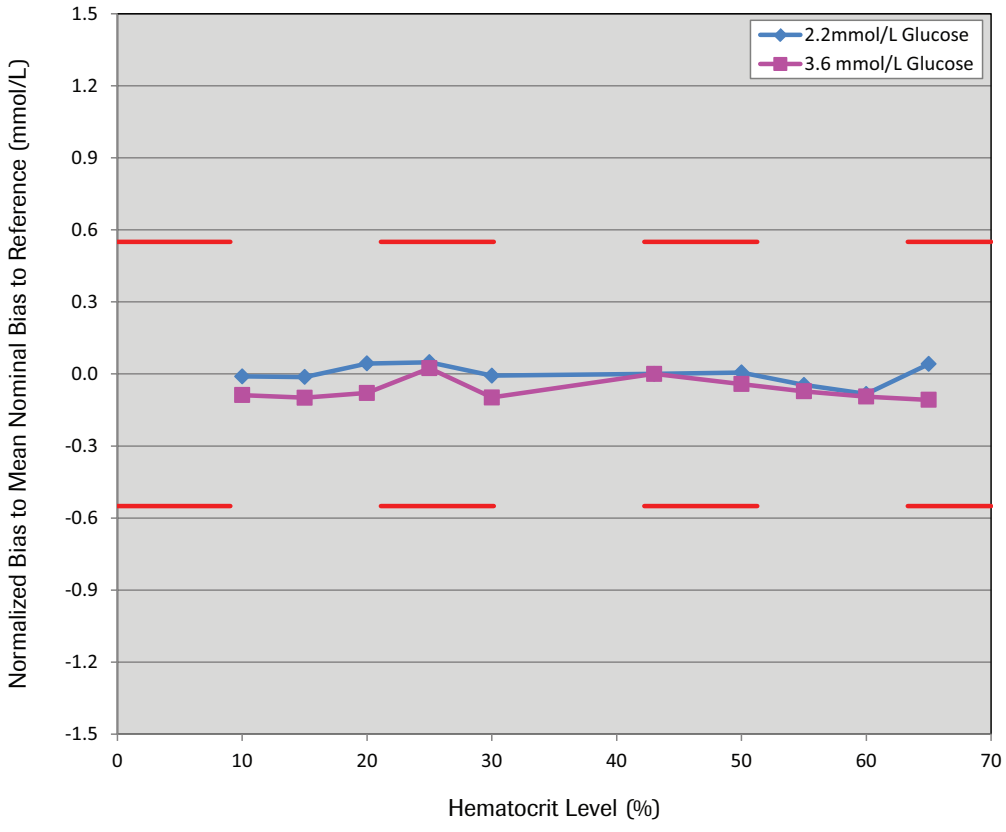
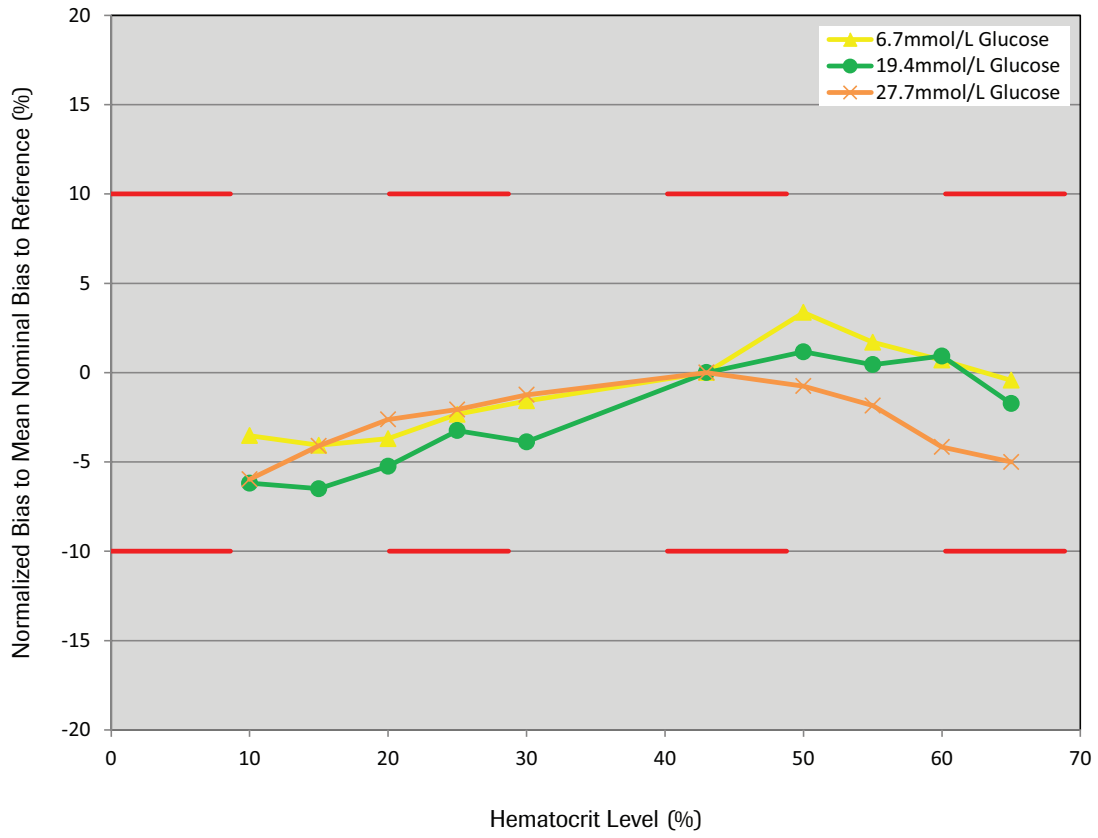


Figure 9. Impact of Hematocrit – Mid and High Glucose Concentrations



Interfering Substances

The Accu-Chek Aviva system has been thoroughly evaluated with potential interfering substances. Substances specified in Annex A of the ISO (International Organization for Standardization) 15197:2013 Standard were tested at concentrations described by the Clinical Lab Standard Institute (CLSI) in document EP7-A2 — *Interference Testing in Clinical Chemistry; Approved Guideline*, when available. Many of the endogenous and exogenous elements were evaluated at strengths three or more times therapeutic plasma concentrations. Each medication and metabolite was evaluated at the following targeted glucose levels to ensure accuracy:

- 2.8 to 5.6 mmol/L
- 13.9 to 19.4 mmol/L

Test results indicate that the Accu-Chek Aviva system provides accurate results in the presence of the substances tested, generally well beyond the therapeutic or physiologic range. See Table 6 for a list of the substances evaluated, along with the concentration tested and the therapeutic or physiologic concentration range (or upper limit). All concentrations are in terms of mmol/L unless noted otherwise.

Table 6. Potential Interfering Substances – Concentrations Tested

Substance	Concentration Tested (mmol/L)	Therapeutic / Physiologic Concentration Range (or Upper Limit) (mmol/L)
Acetaminophen	1.32	0.066 – 0.199
Bilirubin (unconjugated)	0.68	0.019
Cholesterol	12.93	7.75
Creatinine	2.65	0.13
DOPA (L)	0.10	0.001 – 0.014
Dopamine	0.0059	0.002
EDTA (K2)	9.62	N/A[1]
Gentisic Acid	0.116	0.013 – 0.039
Glutathione (reduced)	0.20	0.02
Hemoglobin	0.088	0.0016
Heparin (Li)	8000 U/dL	35 – 100 U/dL
Ibuprofen	2.42	0.049 – 0.34
Maltose	10.52	0 – 10.52
Methyl Dopa	0.07	0.0047 – 0.036
Salicylic Acid	4.54	0.72 – 2.17
Tolazamide	6.42	0.05
Tolbutamide	3.70	0.16 – 0.89
Uric Acid	1.40	0.14 – 0.48
Xylose	6.66	2

[1] EDTA (K2) is used as an anticoagulant in blood collection tubes.

The following compounds, when tested with the Accu-Chek Aviva system, were found to be interfering substances.

Table 7. Interfering Substances

Substance	Accu-Chek Aviva System Accuracy Threshold (mmol/L)
Lipidemia (Triglycerides)[2]	> 20.3
Galactose[3]	> 0.83
Ascorbic Acid[4]	> 0.17

[2] Lipemic samples (triglycerides) in excess of 20.3 mmol/L may produce elevated results.

[3] Blood concentrations of galactose greater than 0.83 mmol/L will cause overestimation of blood glucose results. Glucose values in neonates suspect for galactosemia should be confirmed by an alternate glucose methodology.

[4] Intravenous administration of ascorbic acid that results in blood concentrations of ascorbic acid greater than 0.17 mmol/L will cause overestimation of blood glucose results.

Conclusion

The data presented in this document demonstrate the capability of the Accu-Chek Aviva meter and test strips with advanced chemistry. The system's 5-second test, wide hematocrit and environmental ranges, and minimal sample volume make it an easy-to-use tool for monitoring of blood glucose levels. With every test, the system performs extensive quality checks to ensure accurate and reliable results. The system's advanced chemistry also provides accurate test results in the presence of maltose, which makes it suitable for use by people receiving therapy with solutions containing or producing maltose.