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ALERE EXECUTIVE SUMMARY

Prepared for the
July 22, 2016 meeting of the
Clinical Chemistry and Clinical Toxicology Devices Panel
k153726
Afinion HbA1c Dx Test System
Alere Technologies AS

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1. SUMMARY

The Office of In Vitro Diagnostics and Radiological Health (OIR) within the Food and Drug Administration's (FDA) Center for Devices and Radiological Health (CDRH) has requested feedback from the clinical community in a public panel meeting with respect to the proposed use of the Alere Afinion™ HbA1c Dx test as an aid in the diagnosis of diabetes and pre-diabetes in clinical laboratories and point-of-care (POC) laboratory settings. The information that follows supports Alere's position that the Afinion HbA1c Dx test is safe and effective for its proposed intended use and that the product is substantially equivalent to the predicate device (Cobas C501 Tina-Quant HbA1cDx Gen.3 assay (k121610)) identified in the premarket notification submitted to FDA.

The Afinion HbA1c Dx test is proposed as a CLIA (Clinical Laboratory Improvements Amendment) moderate complexity test for the quantitative determination of glycated hemoglobin (% hemoglobin A1c, HbA1c) to be used as an aid in the diagnosis of diabetes, and for identifying patients who may be at risk for developing diabetes. According to the recommendations of the American Diabetes Association (ADA), values at or above 6.5 % HbA1c (DCCT /NGSP) are suitable for the diagnosis of diabetes mellitus. Patients with HbA1c values in the range of 5.7-6.4 % HbA1c (DCCT/NGSP)[a] may be at a risk of developing diabetes[1,2]. In addition to the diagnostic indication, Alere proposes that the Afinion HbA1c Dx test also maintain the same indication as the currently marketed Alere Afinion HbA1c test (k050574): the measurement of %HbA1c as a marker of long-term metabolic control in persons with diabetes mellitus.

[a] The %HbA1c (DCCT/NGSP) units are standardized to Diabetes Control and Complications Trial (DCCT)[3] values by the National Glycohemoglobin Standardization Program (NGSP).

2. DEVICE DESCRIPTION

2.1 Proposed Intended Use

The Alere Afinion™ HbA1c Dx test is an *in vitro* diagnostic test for quantitative determination of glycated hemoglobin (% hemoglobin A1c, HbA1c) in human whole blood.

This test is to be used as an aid in the diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.

The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.

For use in clinical laboratories and point-of-care laboratory settings.

2.2 Principle of the Afinion HbA1c Dx Test

The Afinion HbA1c Dx test is a fully automated boronate affinity assay for the determination of the percentage of hemoglobin A1c in human whole blood. The Afinion HbA1c Dx test cartridge contains all of the reagents necessary for the determination of % HbA1c. A patient specimen is collected with the integrated sampling device then reinserted back into the test cartridge. The test cartridge is then placed in the cartridge chamber of the Afinion AS100 Analyzer. The blood sample is automatically diluted and mixed with a solution that releases hemoglobin from the erythrocytes, precipitating the hemoglobin. This sample mixture is transferred to a blue boronic acid conjugate, which binds to the cis-diols of glycated hemoglobin. This reaction mixture is soaked through a filter membrane and all precipitated hemoglobin, conjugate-bound and unbound (i.e. glycated and non-glycated hemoglobin) remains on the membrane. Any excess conjugate is removed with a washing reagent. The analyzer evaluates the precipitate on the membrane. By measuring the reflectance, the blue (glycated hemoglobin) and the red (total hemoglobin) color intensities are evaluated, the ratio between them is proportional to the percentage of HbA1c in the sample. The % HbA1c is displayed on the Alere Afinion™ AS100 Analyzer.

2.3 Afinion HbA1c Dx Test System

The materials required for performing the Afinion HbA1c Dx test (15 tests per kit) include the following:

- 15 test cartridges packed separately in foil pouches with a desiccant bag
- Package insert

The following additional materials are required to perform the test, but not provided with the test kit:

- Afinion AS100 Analyzer
- Afinion AS100 Analyzer User Manual (provided with the Afinion AS100 Analyzer)
- Afinion HbA1c Dx Quick Guide (provided with the Afinion AS100 Analyzer)
- Afinion HbA1c Control
- Standard blood collection equipment

The Afinion HbA1c Dx test is used with the Afinion AS100 Analyzer, which is pictured in **Figure 2.3-1.**

Figure 2.3-1 Afinion AS100 Analyzer

2.4 Test Procedure

The Afinion AS100 Analyzer is a multi-assay analyzer for clinical laboratory and POC use which utilizes a digital camera and Light Emitting Diodes (LEDs) to perform two kinds of measurements:

- reflection measurement - amount of light reflected from a membrane
- transmission measurement - amount of light propagating through a liquid

The analyzer performs optical, electronic and mechanical checks on the sampling device and the test cartridge as well as during individual processing steps. If the analyzer detects an error, the assay will be interrupted and patient results are not reported. The analyzer displays an information code that can be interpreted by the operator using the analyzer instructions for use. The automatic start-up self-test verifies the hardware and software integrity, the test cartridge transport system, the liquid transport system, and the camera vision system. When the analyzer is switched on for a longer period, it will automatically restart once a day to ensure that a self-test is done regularly.

The analyzer is provided to the user pre-calibrated. Lot specific calibration information is contained in the test cartridge bar code which is read automatically once the test cartridge is inserted into the analyzer.

To perform a test, the integrated sampling device is used to draw up either a patient or control sample by capillary action. The sampling device is re-inserted into the test cartridge and then placed into the cartridge chamber of the analyzer. The lid is closed and the cartridge is transported into the analysis compartment. Test and lot specific information read from the barcode label identifies the test and signals to the analyzer how to process the test cartridge. The sample and reagents are automatically transferred between the wells of the test cartridge. A monochrome solid-state camera monitors the entire process. When the assay is completed, LEDs illuminate the final reaction area located on the filter membrane. The camera detects the reflected light, which is converted to a test result and displayed on the screen. When the user accepts the result, the lid opens and the used cartridge is removed and discarded.

The Afinion AS100 Analyzer has two main user interfaces, the touch screen and the cartridge chamber **(Figure 2.4-1)**. The analyzer is easily operated using the icons that appear on the touch screen. Only the icons needed by the user at each operative step are displayed. Text messages and icons that appear on the screen help guide the user through the testing procedure **(Figure 2.4-2 and 2.4-3)**. **Figure 2.4-4** shows the test cartridge and its components.

Figure 2.4-1 Analyzer touch screen and cartridge chamber

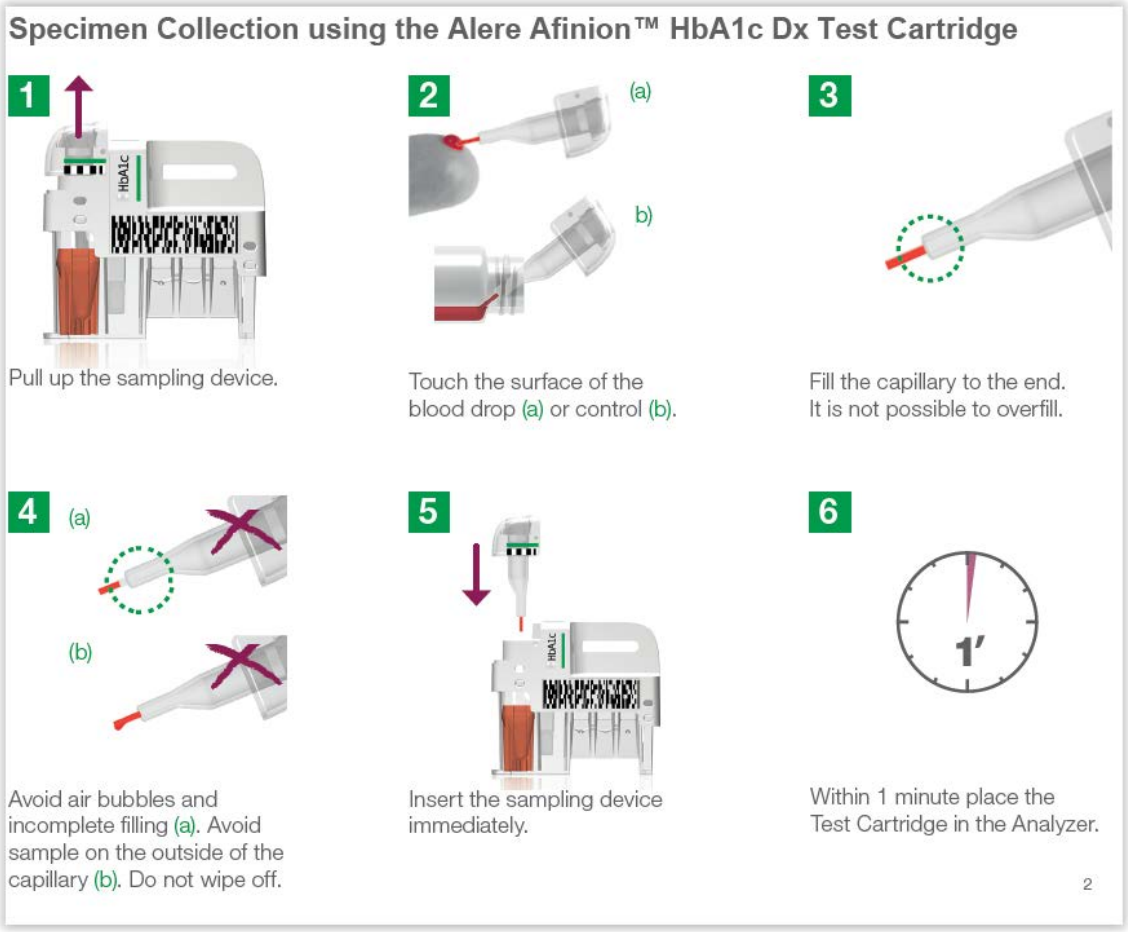


Figure 2.4-2 Illustration of test procedure from quick guide

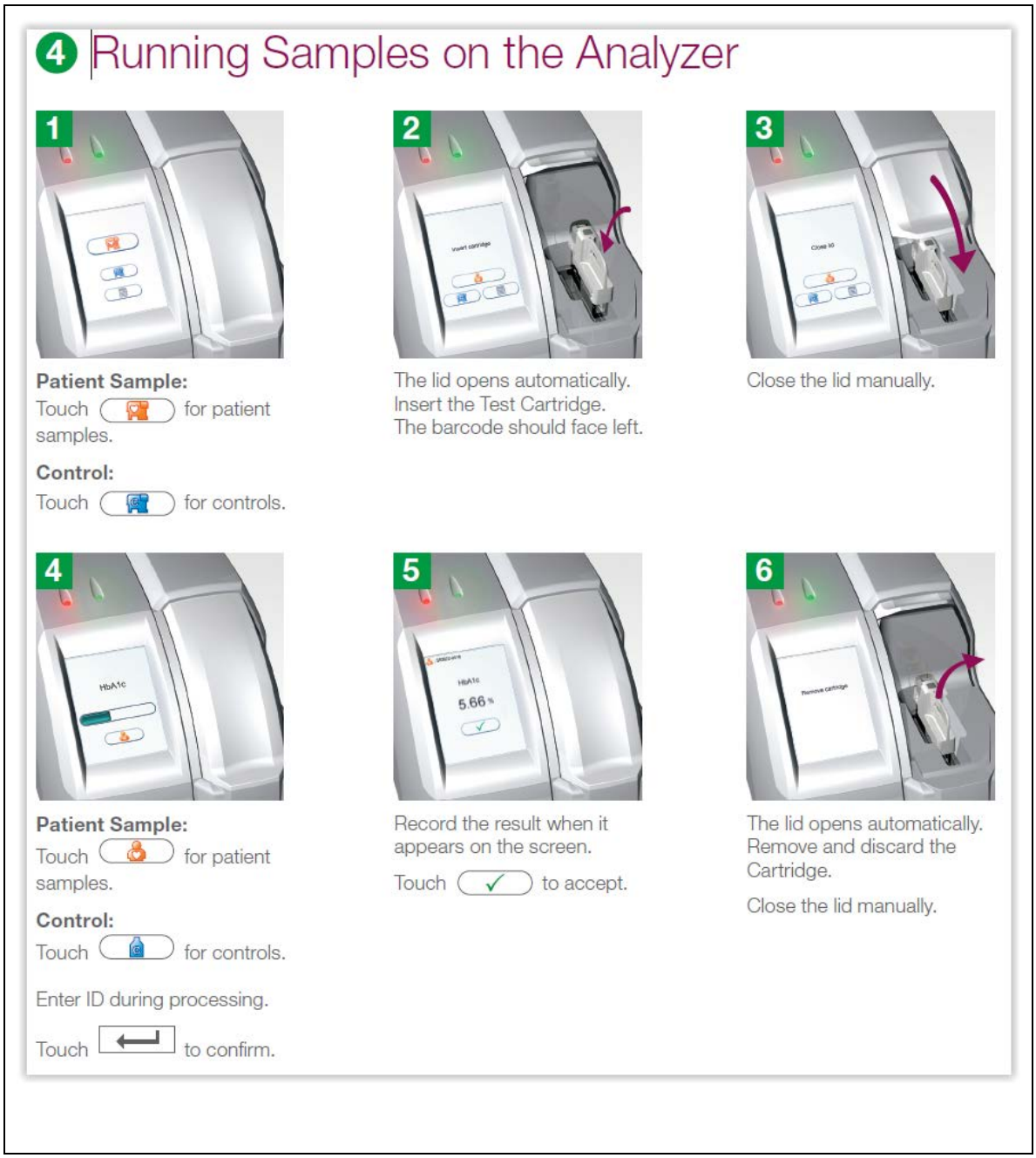
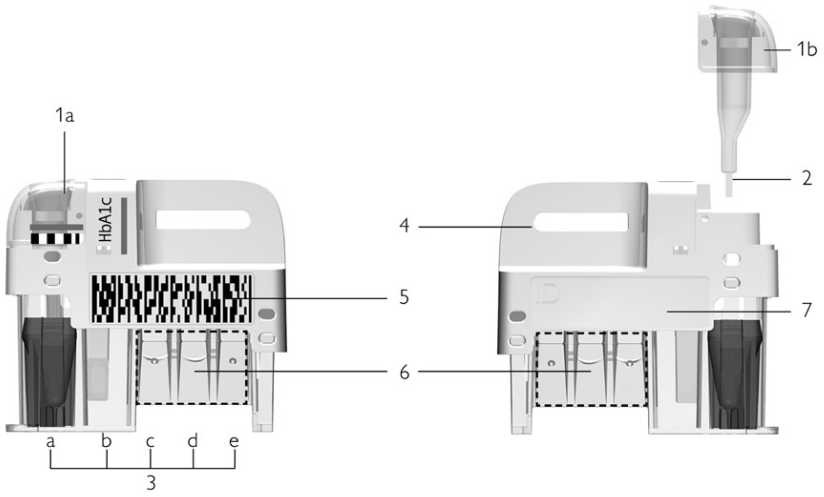


Figure 2.4-3 Illustration of test procedure from quick guide



Component	Function/composition
1a. Sampling device, closed position 1b. Sampling device, lifted position	For collection of patient sample or control.
2 Capillary	1.5 µL capillary to be filled with sample material.
3 Reaction container a. Conjugate b. Membrane tube c. Washing solution d. Reconstitution reagent e. Empty	Contains reagents necessary for one test: Blue boronic acid conjugate. Tube with a polyethersulfone membrane. Morpholine buffered sodium chloride with detergents and preservative. HEPES buffered sodium chloride with lysis and precipitation agents.
4 Handle	For correct place to hold the Test Cartridge.
5 Barcode label	Contains assay and lot specific information for the Analyzer.
6 Optical reading area	Area for transmission measurement.
7 ID area	Space for written or labeled sample identification.

Figure 2.4-4 Afinion HbA1c Dx test cartridge and components

2.5 Afinion HbA1c Controls

The Afinion HbA1c Control kit is 510(k) cleared for use with the Afinion HbA1c system (Afinion HbA1c test cartridges and Afinion AS100 Analyzer). It includes two control samples with different HbA1c level target values as follows:

1. Afinion HbA1c Control C I (1 x 0.5 mL)
    - Target % HbA1c level: 5.0-6.5
    - Stabilized preparation from porcine whole blood
2. Afinion HbA1c Control C II (1 x 0.5 mL)
    - Target % HbA1c level: 7.7-11.0
    - Stabilized preparation from human whole blood

The proposed labeling for the Afinion HbA1c Dx test will include the following information regarding frequency of quality control testing:

"Controls should be analyzed:

- *With each new shipment of Alere Afinion™ HbA1c Dx test kits.*
- *With each new lot of Alere Afinion™ HbA1c Dx test kits.*
- *At least every 30 days.*
- *When training new operators in correct use of the Alere Afinion™ HbA1c Dx and the Alere Afinion™ AS100 Analyzer.*
- *Anytime an unexpected test result is obtained*

If local, state and/or federal regulations require more frequent testing of control materials, then quality control should be performed in compliance with these regulations."

The Afinion AS100 Analyzer User Manual has the following additional recommendations:

"Controls should be analyzed:

- *When starting up an Alere Afinion AS100 Analyzer for the first time.*
- *After software upgrade of the Alere Afinion AS100 Analyzer.*

Each laboratory site can benefit from establishing a quality control plan. The laboratory director should determine whether additional testing is appropriate for their laboratory."

2.6 Additional System Control Features

The Afinion AS100 Analyzer User Manual describes the configuration of the optional patient ID, operator ID and quality control lock out functionalities by using the touch screen configuration menu.

Patient ID

The Alere Afinion AS100 Analyzer patient ID functionality will, if configured, allow up to four patient ID fields to be entered per test run. The Patient ID will be stored with each patient test result in the result records.

Operator ID

The Alere Afinion AS100 Analyzer operator functionality will, if configured, require the operators to login before testing. The functionality may also prevent un-authorized operators to login, perform tests and configuration. The operator ID will be stored with each test result in the result records.

Quality Control Lockout

The Alere Afinion AS100 Analyzer QC lockout function allows the user to configure the instrument to automatically enforce the required frequency of control testing according to applicable regulations and local quality plan. If the required control test has not been performed or the control result is outside the acceptable range, the instrument will disable patient testing for this assay.

2.7 NGSP Certification

National Glycohemoglobin Standardization Program (NGSP) certification currently requires that an HbA1c method perform within 6% (relative) total error with respect to a reference laboratory method performed by an NGSP certified laboratory for a panel of representative patient samples (http://www.ngsp.org/critsumm.asp). The Afinion AS100 Analyzer and the currently marketed Afinion HbA1c test have been NGSP certified every year since commercial introduction in 2006. Certification of the Afinion HbA1c Dx test was successfully completed in 2016.

2.8 Configuration Management

The Afinion HbA1c Dx test, which is proposed as a CLIA moderate complexity test, will be distinguished from the currently marketed CLIA-waived Alere Afinion HbA1c test. Two US market configurations of Alere Afinion AS100 Analyzer will be available at launch of Alere Afinion HbA1c Dx test: CLIA waived and moderate complexity. The products will have different names, catalogue numbers, and package inserts. At test start-up for the CLIA waived product, the screen will display "CLIA WAIVED."

In addition, the CLIA waived market configuration will use cartridge barcode recognition technology to ensure that only CLIA waived assays can be run on the CLIA waived version of the analyzer. Whereas the moderate complexity market configuration will run both CLIA waived and non-CLIA waived Afinion assays, the Alere Afinion HbA1c Dx test will be incapable of being run on the CLIA waived market configuration of the analyzer. If an Afinion HbA1c Dx cartridge is inserted into a currently installed Afinion AS100 Analyzer with the current software version, the analyzer will not perform the test and instead an information code will be displayed.

3. PRODUCT PERFORMANCE

Alere has submitted detailed performance data to FDA in the 510(k) premarket notification for the Afinion HbA1c Dx test. These data for precision, accuracy, total error and assay interferences applicable to the FDA special controls (see Section 5, Table 5.1-2) are summarized below. The 510(k) Summary in Tab 6 provides a high-level discussion of the content of the premarket submission.

The performance of the Afinion HbA1c Dx test will be reviewed by FDA for a determination of substantial equivalence to the predicate device. While FDA is not seeking the panel's input on the question of substantial equivalence, Alere believes that product performance is relevant to the panel's opinion on the suitability of the Afinion HbA1c Dx assay to aid in the diagnose of diabetes in moderate complexity POC laboratories.

3.1 Precision

Precision – Venous Whole Blood

The precision of the Afinion HbA1c Dx was evaluated externally. Four levels of HbA1c in anticoagulated venous whole blood patient samples at the following targeted HbA1c values: 5, 6.5, 8 and 12 %HbA1c, were evaluated at each of three study sites. The three study sites were representative of a POC setting and CLIA certified to conduct moderate complexity testing. A total of eight trained medical professional operators participated in the study. Two controls, Alere Afinion HbA1c Controls CI and CII, and three test cartridge lots were included in the study. Four replicates of venous whole blood and the two controls were analyzed twice a day for ten days with each of the three lots at each of the three sites. Precision was evaluated over 10 days since the Afinion HbA1c Dx can only use fresh venous whole blood, and not frozen samples. HbA1c is stable in refrigerated fresh venous whole blood samples for 10 days. The number of replicates per run was doubled to ensure that the same number of measurements as required by 21 CFR 862.1373 Special Controls (2 replicates per run, 2 runs per day for 20 days), were obtained.

Table 3.1-1 External precision - results from site 1

Level	Mean	Repeatability		Between run		Between day		Between lot		Total	
	%HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.08	0.061	1.20	0.000	0.00	0.000	0.00	0.034	0.67	0.070	1.38
Threshold	6.44	0.080	1.24	0.013	0.20	0.000	0.00	0.042	0.65	0.091	1.41
Medium	8.48	0.101	1.19	0.000	0.00	0.000	0.00	0.029	0.34	0.105	1.24
High	12.11	0.140	1.16	0.000	0.00	0.000	0.00	0.000	0.00	0.140	1.16
C I	6.35	0.052	0.82	0.000	0.00	0.017	0.27	0.024	0.38	0.060	0.95
C II	8.51	0.063	0.74	0.000	0.00	0.010	0.12	0.000	0.00	0.064	0.75

Table 3.1-2: External precision - results from site 2

Level	Mean	Repeatability		Between run		Between day		Between lot		Total	
	%HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.24	0.073	1.39	0.018	0.34	0.000	0.00	0.030	0.57	0.081	1.55
Threshold	6.18	0.061	0.99	0.000	0.00	0.000	0.00	0.047	0.76	0.077	1.25
Medium	7.90	0.082	1.04	0.000	0.00	0.005	0.06	0.041	0.52	0.092	1.16
High	12.36	0.101	0.82	0.029	0.24	0.000	0.00	0.000	0.00	0.105	0.85
C I	6.31	0.063	1.00	0.000	0.00	0.000	0.00	0.018	0.29	0.066	1.05
C II	8.45	0.068	0.80	0.000	0.00	0.000	0.00	0.000	0.00	0.068	0.80

Table 3.1-3: External precision - results from site 3

Level	Mean	Repeatability		Between run		Between day		Between lot		Total	
	%HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	4.74	0.048	1.01	0.000	0.00	0.011	0.23	0.045	0.95	0.067	1.41
Threshold	6.62	0.073	1.10	0.000	0.00	0.011	0.17	0.000	0.00	0.074	1.12
Medium	8.15	0.088	1.08	0.000	0.00	0.000	0.00	0.000	0.00	0.088	1.08
High	11.81	0.108	0.92	0.000	0.00	0.000	0.00	0.000	0.00	0.108	0.92
C I	6.31	0.052	0.82	0.000	0.00	0.000	0.00	0.000	0.00	0.052	0.82
C II	8.46	0.069	0.82	0.000	0.00	0.000	0.00	0.000	0.00	0.069	0.82

Table 3.1-4: External precision - combined results (Root Mean Squared SD and %CV)

	Mean	Repeatability		Between run		Between day		Between lot		Total	
Level	%HbA1c	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.02	0.061	1.21	0.010	0.20	0.007	0.13	0.038	0.75	0.073	1.45
Threshold	6.41	0.072	1.12	0.007	0.12	0.006	0.10	0.037	0.58	0.081	1.27
Medium	8.18	0.090	1.11	0.000	0.00	0.003	0.04	0.029	0.36	0.095	1.16
High	12.09	0.118	0.97	0.016	0.14	0.000	0.00	0.000	0.00	0.119	0.98
C I	6.32	0.056	0.89	0.000	0.00	0.010	0.16	0.017	0.27	0.060	0.94
C II	8.48	0.067	0.79	0.000	0.00	0.006	0.07	0.000	0.00	0.067	0.79

Precision - Fingerstick Whole Blood

To examine the precision of the assay with fingerstick whole blood samples, a retrospective analysis was conducted utilizing the data available from the external method comparison (see section 3.2). Duplicate fingerstick whole blood samples from 172 subjects were collected and evaluated. The duplicate analyses were grouped in four bins (levels) of %HbA1c. The CV for each bin was estimated by taking the root mean square (RMS) of the pairwise SD within each bin and dividing by the mean of each bin. The percent CV values observed for fingerstick whole blood samples are similar to those observed for venous whole blood samples. The data are presented in **Table 3.1-5** below**.**

Table 3.1-5: Precision of fingerstick whole blood samples:

%HbA1c Levels	No. of samples	Minimum %HbA1c	Maximum %HbA1c	Average %HbA1c	Sr	CV (%)
4.00-5.99	**47**	**4.77**	**5.99**	**5.41**	**0.103**	**1.90**
6.00-6.99	**68**	**6.00**	**6.98**	**6.46**	**0.090**	**1.40**
7.00-9.99	**51**	**7.02**	**9.94**	**7.93**	**0.106**	**1.33**
≥10	**6**	**10.07**	**11.52**	**10.72**	**0.059**	**0.55**

3.2 Accuracy – Fingerstick and Venous Whole Blood

A method comparison (accuracy study) was performed using an NGSP secondary reference laboratory method (Tosoh Glycohemoglobin test on the G8 HPLC analyzer) as the comparator (reference) method. Three production lots of Alere Afinion HbA1c Dx test cartridges were evaluated with two lots assigned to each of the three study sites. The three study sites were representative of a POC setting and CLIA certified to conduct moderate complexity testing. A total of 10 trained medical professional operators participated in the study. Fingerstick samples and fresh venous EDTA samples were obtained from a total of 120 subjects and tested as single replicates per lot. The sample concentrations were in the range of 4.66 to 11.58 %HbA1c. Parameters from Weighted Deming regression are shown in **Table 3.2-1** for results across three lots and three sites, and estimated bias at four levels of %HbA1c are shown in **Table 3.2-2**. Graphical presentations of the results are included in **Figures 3.2-1, 3.2-2 and 3.2-3.**

Table 3.2-1: Weighted Deming regression –combined results - 3 sites and 3 lots

	Fingerstick whole blood	**Venous whole blood**
Slope	0.997	0.991
Slope - 95% confidence interval	0.966 to 1.027	0.959 to 1.022
Intercept	0.000	0.053
Intercept – 95% confidence interval	-0.209 to 0.201	-0.162 to 0.270
Correlation coefficient (R)	0.991	0.990
Number of samples	120	120

Table 3.2-2: Bias and % bias at decision points 5.0, 6.5, 8.0 and at 12.0 %HBA1c for fingerstick and venous whole blood samples, referenced to NGSP results.

	Fingerstick whole blood		**Venous whole blood**	
Decision level (%HbA1c)	Bias (%HbA1c)	% (relative) bias	Bias (%HbA1c)	% (relative) bias
5	-0.02	-0.335	0.01	0.195
6.5	-0.02	-0.334	0.00	-0.052
8	-0.03	-0.334	-0.02	-0.206
12	-0.04	-0.333	-0.05	-0.429

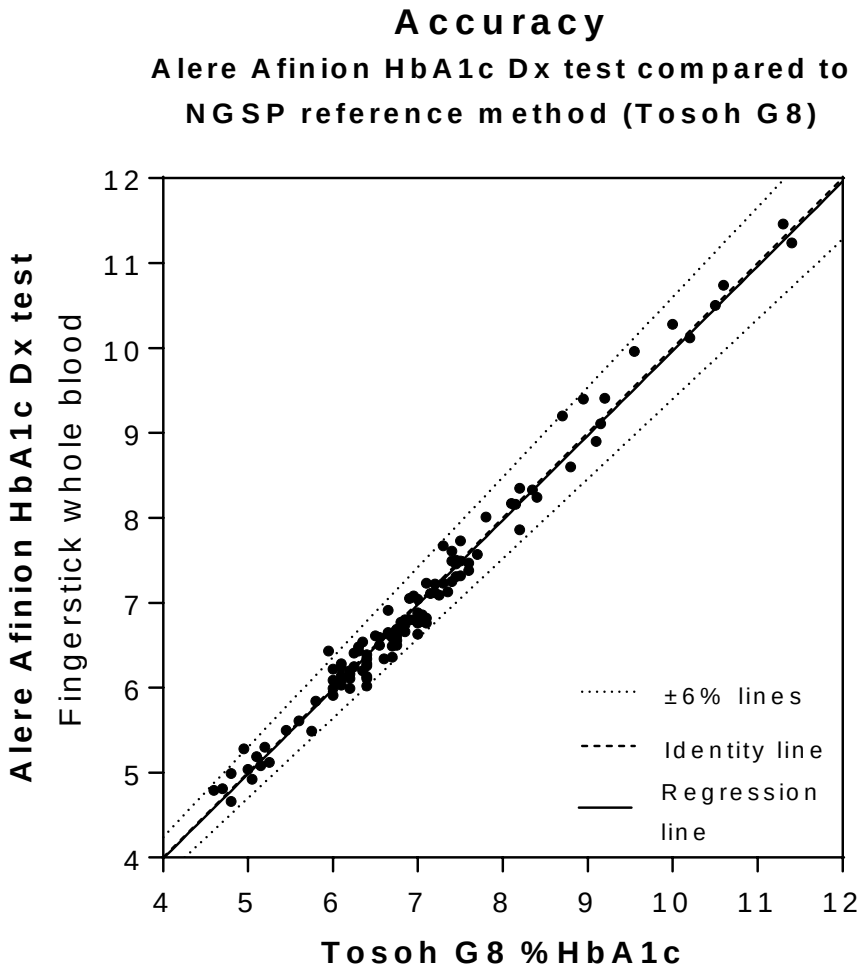


Figure 3.2-1: Accuracy of Afinion HbA1c Dx test compared to the NGSP reference method (Tosoh Glycohemoglobin test on the G8 HPLC analyzer). The Tosoh results are average of two replicates, while the Afinion results are single replicates with fingerstick whole blood samples. n=120.

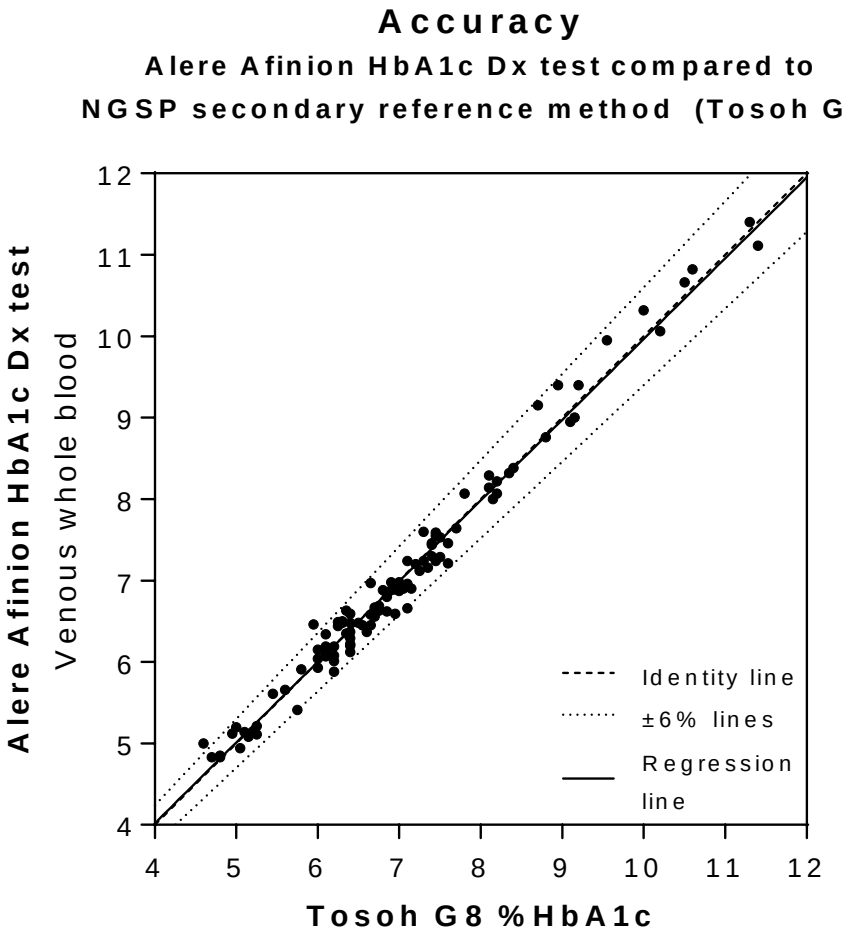


Figure 3.2-2: Accuracy of Afinion HbA1c Dx test compared to the NGSP reference method (Tosoh Glycohemoglobin test on the G8 HPLC analyzer). The Tosoh results are average of two replicates, while the Afinion results are single replicates with venous whole blood samples. n=120.

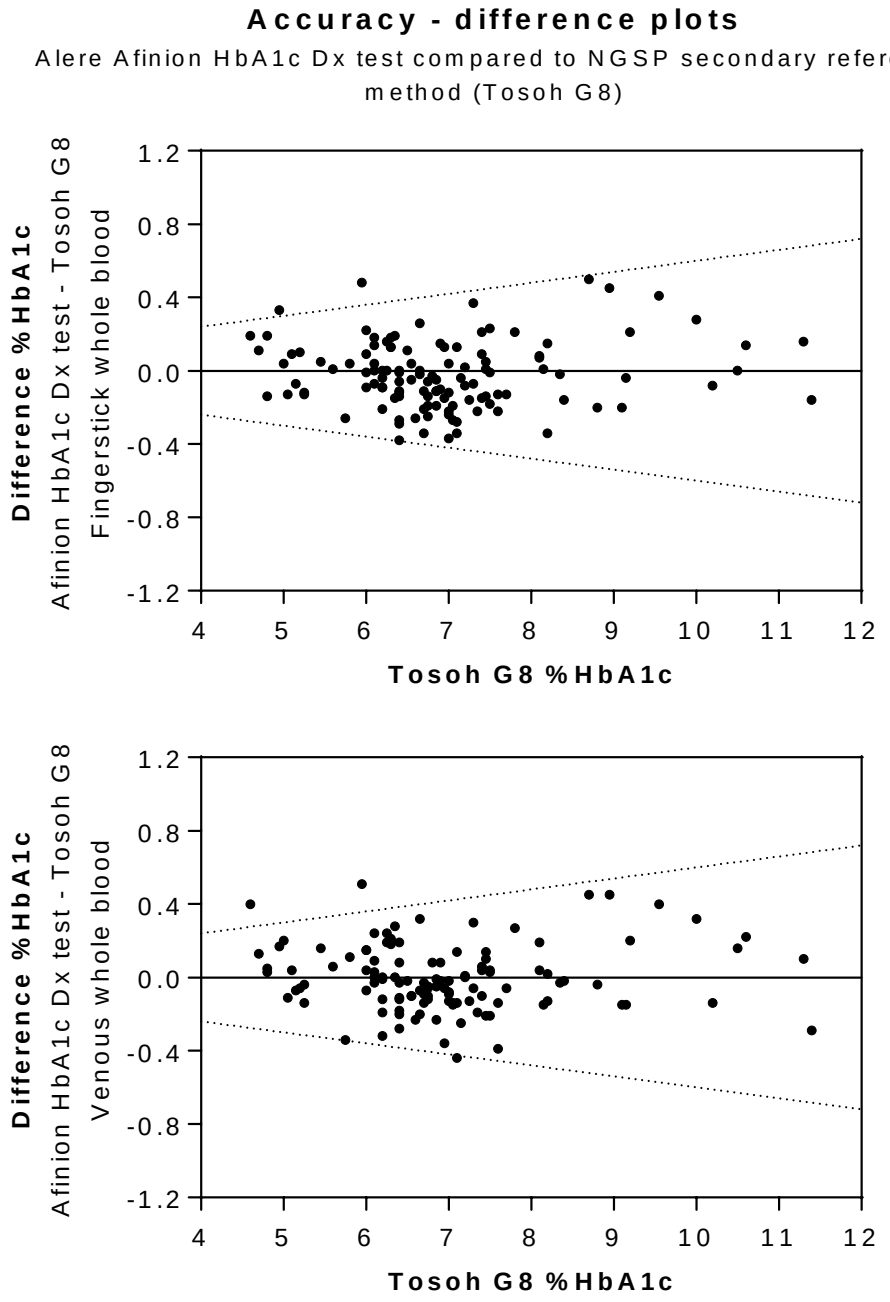


Figure 3.2-3: Difference plots illustrating the accuracy of Afinion HbA1c Dx test compared to the NGSP reference method (Tosoh Glycohemoglobin test on the G8 HPLC analyzer). The Tosoh results are average of two replicates, while the Afinion results are single replicates with venous whole blood samples. n=120. Difference is shown in %HbA1c units. Dotted lines are the ±6% lines.

These data illustrate a high degree of accuracy for the Afinion HbA1c Dx test compared to the NGSP reference method (Tosoh Glycohemoglobin test on the G8 HPLC analyzer).

The accuracy results for each of the three different manufacturing lots of the Afinion HbA1c Dx test are shown in **Figure 3.2-4**. The regression lines for the comparison to the NGSP reference method are not significantly different for all three of the lots.

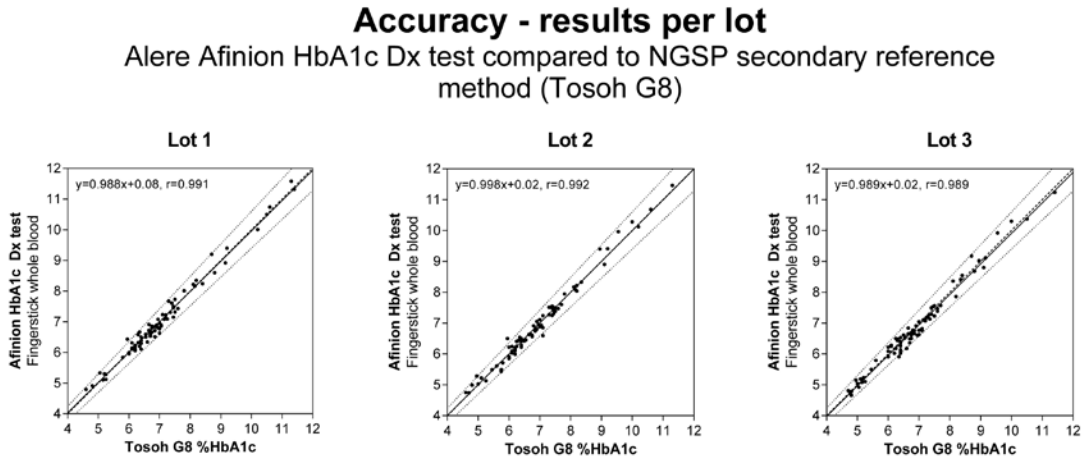


Figure 3.2-4: Accuracy of Afinion HbA1c Dx **test compared to** the NGSP reference method (Tosoh Glycohemoglobin test on the G8 HPLC analyzer) for three different manufacturing lots. The Tosoh results are average of two replicates, while the Afinion results are single replicates with venous whole blood samples. N≈ 80 per lot.

3.3 Total Error

Using the results of bias estimation (%Bias) from the accuracy study and precision estimates (%CV) in the precision study from the three study sites, the percent total error (%TE) at four concentrations (5.0, 6.5, 8.0 and 12.0 %HbA1c) was calculated according to equation 1.

$$\%TE = |\%Bias| + 1.96 * \%CV * (1 + \%Bias/100)$$

(Equation 1)

The precision estimates from venous whole blood were used to estimate %TE both for fingerstick samples and venous whole blood samples with an acceptable %TE of ≤6.0%. The data are presented in **Tables 3.3-1 and 3.3-2.** From the retrospective analysis of fingerstick precision estimated from duplicate results obtained in the accuracy study, %TE was calculated and presented in **Table 3.3-3.**

Table 3.3-1: Total error – fingerstick whole blood samples

%HbA1c Level	%Bias	%CV	%TE
5.0	-0.335	1.45	3.16
6.5	-0.334	1.27	2.81
8.0	-0.334	1.16	2.60
12.0	-0.333	0.98	2.25

Table 3.3-2: Total error - venous whole blood samples

%HbA1c Level	%Bias	%CV	%TE
5.0	0.195	1.45	3.04
6.5	-0.052	1.27	2.53
8.0	-0.206	1.16	2.48
12.0	-0.429	0.98	2.35

Table 3.3-3: Total error – fingerstick whole blood samples using fingerstick precision

%HbA1c Level	%Bias	%CV	%TE
5.0	-0.335	1.90	4.05
6.5	-0.334	1.40	3.07
8.0	-0.334	1.33	2.94
12.0	-0.333	0.55	1.41

The special controls for an HbA1c test to gain an indication for use as an aid in the diagnosis of diabetes mellitus and as an aid in identification of patients at risk for developing diabetes mellitus, require that the total error of the device be less than or equal to 6%. The total error estimates for the Afinion HbA1c Dx test based on the venous whole blood precision estimates shown in **Tables 3.3-1** and **3.3-2** range from 2.25% to 3.16%, which meets the acceptance criterion for total error. The total error estimates for the Afinion HbA1c Dx test based on the fingerstick whole blood precision estimates shown in **Table 3.3-3** range from 1.41% to 4.05%, these also meet the acceptance criterion of less than 6%.

3.4 Hemoglobin Variants Interference

A hemoglobin variant interference study was performed pursuant to special controls and based on CLSI guideline EP7-A2. A total of 151 fresh EDTA whole blood samples that contained one of six common hemoglobin variants were included in the study, including all variants specified in the special controls requirements of 21 CFR 862.1373. (see **Table 5.1-2**). All samples were tested with the Afinion HbA1c Dx test and with an NGSP reference method that is known to be free from the hemoglobin interference being tested (Trinity Premier Hb9210 for HbC, HbD,HbE, HbS, HbA2, and ADAMS™ A1c HA-8180V for HbF). The level of Hb variant was determined by the Capillarys 2 Flex Piercing method. Interference effect was assessed by comparing the results from the Afinion HbA1c Dx test to the reference method result for samples with potentially interfering hemoglobin variants. Significant interference was defined as exceeding a 7% change in %HbA1c value from the reference method. **Table 3.4-1** indicates the number, range and concentration of samples and **Table 3.4-2**, results from the study.

Table 3.4-1: Sample profile for hemoglobin variant study

Hemoglobin Variant	Number of samples	Range of % content of variant	Range of concentration in %HbA1c
HbA2	20	4-6	5.8-10.6
HbS	20	37-42	5.6-8.8
HbC	20	31-36	5.5-9.7
HbE	20	17-26	6.1-8.9
HbD	20	39-42	6.1-9.4
HbF	51	2-32	6.2-8.9

Table 3.4-2: Hemoglobin variant results

Hemoglobin Variant	Percent relative bias from reference method at two levels of the HbA1c samples	
	Level 1: ~6.5 %HbA1c	Level 1: ~8.5 %HbA1c
HbA2	-3	-3
HbS	-4	-1
HbC	-5	-2
HbE	4	4
HbD	-2	-3
HbF	Bias exceeds -7% when amount of HbF in the sample exceeds 7%^	

^ A negative bias with HbF is independent of %HbA1c level but proportional to the %HbF content.

No significant interference was observed for HbA2, HbS, HbC, HbE and HbD. For HbF interference, the product labeling includes the following prominent boxed warning in accordance with the FDA special controls:

> This device has significant negative interference with fetal hemoglobin (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF including those with known Heredity Persistence of Fetal Hemoglobin. Refer to the Analytical specificity and Limitations sections in this package insert for details.

Some central laboratory HbA1c testing systems that have already been cleared by the FDA for diagnostic use also have significant interference from fetal Hemoglobin, such as the Abbott Architect, Ortho Vitros, Roche Cobas c 501 Tina-quant Gen.3 and the Roche Cobas Integra 800 Tina-quant Gen.2.

4. BENEFITS AND RISKS OF THE HBA1C DX TEST

4.1 Fail-Safe and Failure Alert Mechanisms

The currently marketed Afinion HbA1c test system was cleared in 2005 (k050574) and CLIA waived by application in 2006. As a CLIA waived test, the Afinion HbA1c test was designed to meet the requirements for waived testing laboratories and contains effective mitigations to the risk of an erroneous result. The Afinion HbA1c Dx test components and test procedure are unchanged from the currently marketed Afinion HbA1c test, and therefore the Afinion HbA1c Dx test contains the same mitigations. These are:

- Quick test (about 3.5 minutes assay time)
- Simple to use test system requiring minimum training and education
- The instrument and assay are factory calibrated - no user calibration required
- Robust test system with respect to operator handling and environment (temperature and humidity)
- Analyzer self-test during start-up to ensures it is operating according to specifications
- No maintenance requirements
- Test cartridge with integrated sampling device minimizes risk of contamination and simplifies testing procedure
- The assay requires a small sample volume (1.5 µL venous whole blood or fingerstick sample)
- The test cartridge is a closed system; safe and hygienic to use
- 100% comprehensive quality control testing of every analyzer prior to release

Many fail-safe mechanisms are employed by the Afinion HbA1c Dx test system during test processing. An overview of the main fail-safe mechanisms that mitigate potential sources of operator error is presented in **Table 4.1-1**.

Table 4.1-1: Integrated Fail-Safe Mechanisms of Afinion HbA1c Dx test

Procedural Step		Analyzer Mechanism	Description	Information Code Displayed on Analyzer Screen
1	Instrument start-up	a) The Analyzer performs a self-test each time the instrument is turned on or every 24 hours.	a) The self-test checks the integrity of the camera, pumps, pressure sensors, temperature sensor and the mechanical parts. The instrument will go into a non-operative mode if the self-test specifications are not met.	a) Code 302 – non-operative mode.
2	Sample collection a) Use whole blood samples b) Fill the capillary completely to the end	a) Sample type inspection by use of camera. Image is compared to a reference. b) Volume inspection by use of camera. Image is compared to a reference.	a) Ensures that only whole blood samples are used. Cartridge is rejected with no HbA1c result provided if specifications are not met. b) Ensures that the capillary is filled end-to-end, that there is no short filling, excess sample on the outside of the capillary or air bubbles. Cartridge is rejected with no HbA1c result provided if specifications are not met.	a) Code 203 – wrong sample material b) Code 201 – insufficient sample or Code 202 excess sample
3	Place the test cartridge in the Analyzer within 1 minute after sample collection	Sample integrity inspection Time, volume and pressure inspections monitor the processing steps	Test cartridges with dried or coagulated sample materials will be rejected with no HbA1c result provided	Code 204 – coagulated samples, Code 215 and Code 217 – hemolyzed sample or poor sample quality
4	The test cartridge processing starts automatically	a) Barcode inspection by use of camera b) Time, temperature, volume and pressure inspections monitors the processing steps	a) Expired test cartridges are rejected with no HbA1c result provided b) Ensures that each processing step is successful and for any processing error the test is aborted with no HbA1c result provided	a) Code 209 -Expired test cartridge b) Code 210/211 – Test cartridge temperature too low/high c) Code dependent on processing step and cause of assay abortion

When the **a**nalyzer fail-safe mechanisms detect an error, a unique information code is displayed on the touchscreen. The operator can refer to the analyzer operator manual for further information regarding the nature and origin of the error and the possible actions that can be taken.

4.2 Sources of Hazard and Mitigations

There are several possible sources of error as have been addressed through risk assessment and listed above. Further details and descriptions of the possible hazards and mitigation are provided in the following sub-sections.

4.2.1 Incorrect Cartridge Storage Conditions

This source of potential error has been mitigated by labelling that clearly instructs product storage temperatures and duration on the cartridge boxes and an in the package insert. Alere has validated storage conditions that exceed those stated in the labeling to establish robustness of the product in the event product is incorrectly stored. In validation testing, the cartridges did not fail after storage at extreme conditions, which are not expected to be encountered in any of the POC settings anticipated for use. Should there be a condition that compromises the test cartridge such that the reagent volumes are altered it would be detected by several redundant analyser fail-safe mechanisms. One of these fail-safe mechanisms is a precise camera visual inspection of the reagent volumes. If these reagent volumes are found to be outside of specification, an information code is provided, instead of an erroneous result. No MDRs (Medical Device Reports) have been reported from the market as a result of compromised test cartridges in 10 years of use.

4.2.2 Compromised Sample

A compromised sample that has a high degree of hemolysis is another potential source of error. A hemolyzed sample when applied to a test cartridge will exhibit differences in the flow rate through the cartridge membrane. The analyzer includes a fail-safe mechanism to report an information code instead of a result if such differences in assay processing are observed.

4.2.3 Incorrect Operating Conditions

The analyzer operates at conditions between 15 and 32°C (59 - 89°F) and the test itself operates at conditions between 18 and 30°C (64 - 86°F). The test results are not dependent on temperature when the test cartridge is operated within the specified operating conditions. In the event that the ambient temperature conditions are outside of the analyzer operating temperature range, the instrument will render itself inoperable. The analyzer will also measure the cartridge temperature once inserted into the analyzer. Should the cartridge temperature be outside of the limits for the Afinion HbA1c Dx test, the test will be aborted and an information code will be displayed. The analyzer functioning has also been validated for relative humidity conditions ranging from 10% to 90% (non-condensing). If the humidity conditions are outside of this range, an information code will be displayed.

4.2.4 Incorrect User Operation

Another possible source of error is the incorrect use of the Afinion analyzer by the operator. Quality control testing is performed on each and every instrument prior to release. Operator intervention to alter the calibration of the instrument is not possible due to fixed factory calibration that cannot be modified by the end user. In addition, an instrument self-test at start-up, or every 24 hours, occurs to monitor system integrity, rendering the instrument inoperable if it is out of specification. In the 10 years that Afinion analyzer systems have been commercially available, no drifts in calibration have been observed. New instruments manufactured today share the exact performance of the retained instruments from the first ones released into the market 10 years ago. There have been no MDRs (Medical Device Reports) associated with an erroneous results arising from compromised instruments in the market over 10 years in use.

Even when an instrument is properly calibrated, operators can introduce error. The first and most important mitigation is that the test procedure is extremely simple as shown in **Figure 4.2.4-1** below:

Figure 4.2.4-1 Test Procedure

Despite the design of the sampling device which makes the sample collection process simple, it is possible that operators may potentially (in rare cases) under-fill or introduce bubbles into the sample. The operator may also inadvertently cause excess sample on the capillary exterior itself, or break the capillary when reinserting the sampling device into the test cartridge.

Of note, however, the Afinion HbA1c Dx test is not affected by imprecise sampling or variations in sample volume because the HbA1c result is a ratio within a given sample (how much glycated hemoglobin is present as a percentage of overall hemoglobin present). Thus, the possible problems outlined in the previous paragraph will not occur with the Afinion HbA1c Dx test. Nonetheless, Alere has incorporated an additional fail-safe into the analyzer, which inspects the sample device upon the initiation of assay processing and returns an information code instead of a result should the sampling be outside of specifications. Because of this design feature, it is highly unlikely an erroneous result will occur due to operator sampling. Additionally, the Afinion analyzer includes the option to set unique codes for given operators in order to ensure that only those operators who have been appropriately trained are permitted to run the analyzer. These operators would be required to enter their unique passcode in order to gain access to the testing functions.

Another source of error could be that operators may also introduce contaminants such as lotion, glove powder and blood on the outside of the test cartridge in the optical reading area. In most cases, since the instrument is taking two images and subtracting the blank from the result, the contaminants would be subtracted out in the baseline. However, to further mitigate this risk, there is a fail-safe mechanism that checks for

uniformity of the detection area. Should this be outside of specification, an information code will be returned instead of a patient result.

Operators may also introduce error by misinterpreting the test result or testing a patient that should not have an HbA1c test performed such as patients with short RBC lifespan, chemotherapy, or surgery that would lower the result. However, this is not unique to POC testing. These types of errors would also be encountered when sending either the patient or the sample to a central laboratory for testing. The Afinion system mitigates against this type of error by providing clear labeling for when the test should be performed.

There is also a potential source of operator error that comes from transcription errors when reporting and recording patient results. This is mitigated because the results of the Afinion HbA1c Dx test are stored in the analyzer's memory for easy recall, verification and printing. Additionally, the analyzer can be connected to the hospital information system for immediate transmission of the patient results into the patient's medical record. Moreover, these sorts or error are less likely to occur in the POC setting because the patient is present or near at the time of testing and the result can be communicated immediately.

4.2.5 Commercialized Product Controls

As a further means of demonstrating and documenting quality control, labeling for the Afinion Analyzer and the Afinion HbA1c Dx test instruct the user to perform periodic external control testing or more frequent control testing as regulated by local, state or federal regulations using the Alere Afinion HbA1c control materials (described in section 2.5). Alternatively an individualized quality control plan (IQCP) can be developed and implemented. The results of external control testing are stored within a separate log within the analyzer in order to allow for convenient review and documentation of these results. This provides further feedback that the system is performing correctly within specifications. There is also a user programmable function for quality control (QC) lock-out. The QC lock out function enables the setting of an interval of required external QC testing that will render the instrument unable to run patient samples until the required external control testing has been performed and that those results are acceptable.

Data from external quality assurance programs inform appropriate quality performance of the Afinion system in settings outside of the clinical laboratory. In a study recently

published by Solvik et al., 99% of all Norwegian GP offices (1288) over six years demonstrated that accuracy and bias of the Afinion HbA1c test as compared to central laboratory systems was equivalent or even better than central laboratory methods.[4]

In the US, proficiency testing data for the Afinion HbA1c test can be reviewed and compared to the performance of central laboratory testing systems. A review of these data shows that the Afinion HbA1c test is at least as good as many previously cleared clinical laboratory systems and, at times, outperforms central laboratory methods.

Wood et al. published a study comparing the performance of the Afinion HbA1c Dx test to the NGSP High performance liquid chromatography (HPLC) reference method in 700 pediatric patients testing CLIA waived clinics in the US.[5] The CV for measurements of whole blood samples for precision analysis was 2% for Afinion and 1% for HPLC. In the patient samples measured at the seven clinic sites, the Afinion generated only a slightly higher HbA1c result than the HPLC (mean difference = +0.15) which was considered to be clinically insignificant.

Paknikar et al. reviewed the performance of the Afinion HbA1c test and central lab systems against the NGSP reference. The study also reviewed the variability in results for these methods from historical CAP proficiency data.[6] The authors concluded that the observed variability of the Afinion system was similar to the bias observed with the central laboratory methods.

4.3 Clinical Benefits and Risks

Diabetes mellitus is a life-threatening disease with 415 million patients affected across the globe.[7] The economic burden of diagnosed diabetes in the US is currently at an estimated $245 billion annually - $176 billion in direct medical costs and $69 billion in reduced productivity.[8] With its increasing incidence and high cost of treatment due to complications and non-compliance, diabetes places an enormous burden on the economic resources of the U.S. healthcare system.[9, 10] The Centers for Disease Control and Prevention (CDC) estimates in their 2014 National Diabetes Statistics Report that 21 million people are diagnosed with diabetes and that 8.1million remain undiagnosed and unaware of their condition. The number of people at risk of developing diabetes is even greater. Once diagnosed, diabetes can be managed effectively to delay or reduce the chronic complications associated with the disease. Alternatively, if prediabetes is diagnosed, the appropriate therapy can be initiated.

Diabetes affects underprivileged and minority groups at a disproportionately high level. These groups often have diminished access to care, and can face major challenges attending medical appointments. The implementation of a 'one-stop-shop' opportunistic approach that enables the assessment of diabetes risk and the implementation of a treatment plan on the occasion of a single visit may well lead to better adherence to a treatment plan at a much lower cost than having to implement multiple office visits.

4.3.1 Risks and Mitigations of False Positives and False Negatives

When considering the benefits of POC testing for HbA1c it is important to also understand the likelihood and risks associated with a false positive (misdiagnosis of diabetes) or false negative test result (missed diagnosis of diabetes). To estimate the likelihood of a mis-diagnosis or false positive result with the Afinion system one should consider the frequency distribution of true HbA1c values in the population and apply the standard 6% allowable total error. The distribution of HbA1c results within the U.S. population can be obtained from the NHANES data for individuals meeting the ADA criteria for diabetes testing (greater than 45 years of age or any age who are obese and have at least one additional diabetes risk factor)[b]. Given the ADA requirement to confirm any diagnosis of diabetes with a second test one has to further consider the likelihood of a second result crossing the diagnostic threshold in error. Given these considerations, the likelihood of an erroneous result crossing the diagnostic threshold (6.5% HbA1c) given a true HbA1c value of 6.1%, is less than 1%. The likelihood of a second erroneous result also crossing the diagnostic threshold given a true value of 6.1% HbA1c, is less than 0.004%. In fact, the likelihood of such a false positive event happening is only increased to a 5% chance of occurrence when the true value of HbA1c is 6.3 or 6.4%.

The clinical significance of a small difference of HbA1c (+/- 6% relative) is further attenuated by the recommended treatment associated with prediabetes (5.7 – 6.4% HbA1c) and diabetes (≥6.5% HbA1c).

[b] The National Health and Nutrition Examination Survey results http://wwwn.cdc.gov/Nchs/Nhanes/2013-2014/GHB_H.htm

The ADA recommends the following treatment plan for patients identified as being at high risk for developing diabetes (ie. having prediabetes):[11]

- *Patients with prediabetes should be referred to an intensive diet and physical activity behavioral counseling program adhering to the tenets of the Diabetes Prevention Program (DPP) targeting a loss of 7% of body weight and should increase their moderate-intensity physical activity (such as brisk walking) to at least 150 min/week.*
- *Follow-up counseling and maintenance programs should be offered for long term success in preventing diabetes. Metformin therapy for prevention of type 2 diabetes should be considered in those with prediabetes, especially in those with BMI .35 kg/m2, those aged 60 years, and women with prior gestational diabetes mellitus.*
- *At least annual monitoring for the development of diabetes in those with prediabetes is suggested.*
- *Screening for and treatment of modifiable risk factors for cardiovascular disease is suggested.*

These recommendations do not vary widely from the ADA recommendations for the treatment of newly diagnosed diabetes. In patients newly diagnosed with diabetes, the ADA recommends:[12]

- *A complete medical evaluation should be performed at the initial visit to confirm the diagnosis and classify diabetes.*
- *Detect diabetes complications and potential comorbid conditions.*
- *Begin patient engagement in the formulation of a care management plan.*
- *Develop a plan for continuing care.*

The ADA recommends that initial treatment for most newly diagnosed type 2 diabetes should start with lifestyle changes. If glycemic goals are not achieved with lifestyle interventions alone then metformin monotherapy should be added.[13]

Since lifestyle changes and possible metformin monotherapy are both relevant for patients at risk of developing diabetes and for patients with newly diagnosed diabetes, the potential hazards resulting from a false positive diagnosis of diabetes based on the error rate and magnitude one can expect from the Afinion HbA1c Dx test is low. Furthermore, metformin has a longstanding evidence base for efficacy and safety and is inexpensive. These low risks and potential hazards are no different than those brought by the central laboratory systems already cleared within the same 6% total error.

Similarly, applying the allowable total error (6%) and NHANES distribution to estimate the likelihood of a false negative event, demonstrates that there is a low chance of missing a diagnosis of diabetes. The chance of a true value of 6.8% HbA1c being classified as below 6.5% HbA1c is 2.8%. This is no different than the error rate expected for a central lab system with a 6% total error. The likelihood of a true value of 6.5%

HbA1c falling below the lower limit for prediabetes (5.7% HbA1c) is negligibly small. Thus if a diagnosis of diabetes is missed, this patient will most certainly be identified as extremely high risk for developing diabetes. Such an individual would receive essentially the same care plan (lifestyle modifications and possibly metformin monotherapy) and should, according to ADA recommendations, be retested in follow-up visits at least annually, usually more frequently. As discussed above, the care plan for such an individual would not be significantly different from that of a newly diagnosed patient.

Notwithstanding the above considerations, it is appreciated that if the total error of a method is less than 6%, such as the <4% total error observed with the Afinion HbA1c Dx test, then the probability of a false positive or false negative result is accordingly lower. Clearance of the Afinion HbA1c Dx test for moderate complexity settings will provide qualified health care providers with an effective and efficient means to diagnose diabetes at the time of an office visit. This, in turn, will allow for the prompt initiation of therapy and thus enhance the likelihood of effective management of diabetes.

5. REGULATORY CONSIDERATIONS

5.1 Regulatory History

The currently marketed Afinion HbA1c system was 510(k) cleared in 2005 (k050574) and CLIA waived by application in 2006. Modifications to the system were later 510(k)-cleared in 2011 and 2015 (k110056 and k151809).

With the exception of the additional intended use (i.e., diagnosis of diabetes or pre-diabetes), the features of the proposed Afinion HbA1c Dx test are largely unchanged from the currently marketed Afinion HbA1c test as shown in **Table 5.1-1** below.

Table 5.1-1: Afinion HbA1c / Afinion HbA1c Dx test Feature Comparison

Feature	Afinion™ HbA1c	Afinion™ HbA1c Dx
Intended Use	The Alere Afinion HbA1c is an *in vitro* diagnostic test for quantitative determination of glycated hemoglobin (% hemoglobin A1c, HbA1c) in human whole blood. The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.	*Same as HbA1c, with the addition of the highlighted portion:* The Alere Afinion HbA1c is an *in vitro* diagnostic test for quantitative determination of glycated hemoglobin (% hemoglobin A1c, HbA1c) in human whole blood. This test is to be used as an aid in the diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes. The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.
Test Cartridge	Same except for labeling	
Controls	Same	
Analyzer	Same except for labeling, catalogue numbers and available test menu	
Software	Test results displaying in one decimal	Test results displaying in two decimals
CLIA complexity	Waived	Moderate

The Afinion HbA1c Dx test is proposed as a Class II (special controls) device under 21 CFR 862.1373 (Hemoglobin A1c test system), product code PDJ. The 510(k) premarket notification that Alere has submitted to FDA contains information, data and labeling to demonstrate that the Afinion HbA1c Dx test meets the special controls requirements of 21 CFR 862.1373 as indicated in **Table 3.1-2** above, in addition to demonstrating substantial equivalence to the predicate device (Cobas C501 Tina-Quant HbA1cDx Gen.3 assay (k121610)).

Table 5.1-2: 21 CFR 862.1373

PART 862 -- CLINICAL CHEMISTRY AND CLINICAL TOXICOLOGY DEVICES **Subpart B--Clinical Chemistry Test Systems** **Sec. 862.1373 Hemoglobin A1c test system**
(a) Identification. A hemoglobin A1c test system is a device used to measure the percentage concentration of hemoglobin A1c in blood. Measurement of hemoglobin A1c is used as an aid in the diagnosis of diabetes mellitus and as an aid in the identification of patients at risk for developing diabetes mellitus.
(b) Classification. Class II (special controls). The special controls for this device are:
(1) The device must have initial and annual standardization verification by a certifying glycohemoglobin standardization organization deemed acceptable by FDA.
(2) The premarket notification submission must include performance testing to evaluate precision, accuracy, linearity, and interference, including the following:
(i) Performance testing of device precision must, at a minimum, use blood samples with concentrations near 5.0 percent, 6.5 percent, 8.0 percent, and 12 percent hemoglobin A1c. This testing must evaluate precision over a minimum of 20 days using at least three lots of the device and three instruments, as applicable.
(ii) Performance testing of device accuracy must include a minimum of 120 blood samples that span the measuring interval of the device and compare results of the new device to results of a standardized test method. Results must demonstrate little or no bias versus the standardized method.
(iii) Total error of the new device must be evaluated using single measurements by the new device compared to results of the standardized test method, and this evaluation must demonstrate a total error less than or equal to 6 percent.
(iv) Performance testing must demonstrate that there is little to no interference from common hemoglobin variants, including Hemoglobin C, Hemoglobin D, Hemoglobin E, Hemoglobin A2, and Hemoglobin S.
(3) When assay interference from Hemoglobin F or interference with other hemoglobin variants with low frequency in the population is observed, a warning statement must be placed in a black box and must appear in all labeling material for these devices describing the interference and any affected populations.

Performance testing of precision and accuracy for the Afinion HbA1c Dx was conducted as specified in 21 CFR 862.1373 and as agreed with FDA during the pre-submission process. The results of the precision study demonstrate that the Afinion HbA1c Dx test is precise across its measurement range and at the diabetes diagnostic cutoff of 6.5%

HbA1c (see section 3.1). A total error less than or equal to 6 percent has been demonstrated for the Afinion HbA1c Dx test. The total error for the Afinion HbA1c Dx test is in the range 1.41 - 4.05% at %HbA1c levels 5.0, 6.5, 8.0 and 12.0 (see section 3.3). All other testing specified in 21 CFR 862.1373 was conducted as indicated in section 3.4.

The performance of the Afinion HbA1c Dx test is substantially equivalent to the predicate (Cobas C501 Tina-Quant HbA1cDx Gen.3 assay (k121610)) in terms of precision, accuracy and total error and interferences as shown in **Table 5.1-3** below

Table 5.1-3: Afinion HbA1c Dx performance compared to predicate (Cobas C501 Tina-Quant HbA1cDx Gen.3 assay)

<table>
<tr><th></th><th>Predicate device: (k121610)
Cobas C501Tina-quant HbA1cDx Gen.3 assay</th><th>Alere Afinion Dx test (k153726)</th></tr>
<tr><td>Precision (Combined CV)</td><td>3 analyzers, 3 lots, 21 days, two replicates per run and 2 runs per day; 4 samples and 2 controls
<table>
<tr><td>Mean %HbA1c</td><td>Total CV%</td></tr>
<tr><td>5.05</td><td>1.9</td></tr>
<tr><td>6.40</td><td>1.7</td></tr>
<tr><td>7.99</td><td>2.1</td></tr>
<tr><td>11.34</td><td>2.0</td></tr>
<tr><td>Control: 5.18</td><td>3.0</td></tr>
<tr><td>Control: 9.49</td><td>1.8</td></tr>
</table></td><td>3 analyzers, 3 lots, 10 days, 4 replicates per run and 2 runs per day; 4 samples and 2 controls
<table>
<tr><td>Mean %HbA1c</td><td>Total CV%</td></tr>
<tr><td>5.02</td><td>1.45</td></tr>
<tr><td>6.41</td><td>1.27</td></tr>
<tr><td>8.18</td><td>1.16</td></tr>
<tr><td>12.09</td><td>0.98</td></tr>
<tr><td>Control: 6.32</td><td>1.09</td></tr>
<tr><td>Control: 8.48</td><td>0.92</td></tr>
</table></td></tr>
<tr><td>Accuracy</td><td>Comparison to NGSP reference lab – Passing Bablok regression; 141 samples
<table>
<tr><td></td><td>Result</td><td>95% CI</td></tr>
<tr><td>Slope</td><td>1.006</td><td>0.983 to 1.031</td></tr>
<tr><td>Intercept</td><td>-0.135</td><td>-0.297 to 0.010</td></tr>
<tr><td></td><td>Bias (%HbA1c)</td><td>Relative bias (%)</td></tr>
<tr><td>Bias at 5.2%</td><td>-0.103</td><td>-1.98</td></tr>
<tr><td>Bias at 6.5%</td><td>-0.094</td><td>-1.45</td></tr>
<tr><td>Bias at 8.0%</td><td>-0.085</td><td>-1.06</td></tr>
</table></td><td>Comparison to NGSP reference lab -Weighted Deming regression; 120 samples: Venous whole blood:
<table>
<tr><td></td><td>Result</td><td>95% CI</td></tr>
<tr><td>Slope</td><td>0.991</td><td>0.959 to 1.022</td></tr>
<tr><td>Intercept</td><td>0.053</td><td>-0.162 to 0.270</td></tr>
<tr><td></td><td>Bias (%HbA1c)</td><td>Relative bias (%)</td></tr>
<tr><td>Bias at 5.0%</td><td>0.010</td><td>0.195</td></tr>
<tr><td>Bias at 6.5%</td><td>-0.003</td><td>-0.052</td></tr>
<tr><td>Bias at 8.0%</td><td>-0.017</td><td>-0.206</td></tr>
<tr><td>Bias at 12%</td><td>-0.051</td><td>-0.429</td></tr>
</table>
Fingerstick whole blood:
<table>
<tr><td></td><td>Result</td><td>95% CI</td></tr>
<tr><td>Slope</td><td>0.997</td><td>0.966 to 1.027</td></tr>
<tr><td>Intercept</td><td>0.000</td><td>-0.209 to 0.201</td></tr>
<tr><td></td><td>Bias (%HbA1c)</td><td>Relative bias (%)</td></tr>
<tr><td>Bias at 5.0%</td><td>-0.017</td><td>-0.335</td></tr>
<tr><td>Bias at 6.5%</td><td>-0.022</td><td>-0.334</td></tr>
<tr><td>Bias at 8.0%</td><td>-0.027</td><td>-0.334</td></tr>
<tr><td>Bias at 12%</td><td>-0.040</td><td>-0.333</td></tr>
</table></td></tr>
</table>

<table>
<tr><th></th><th>Predicate device: (k121610)
Cobas C501Tina-quant HbA1cDx Gen.3 assay</th><th>Alere Afinion Dx test (k153726)</th></tr>
<tr><td>Total Error</td><td>
<table>
<tr><td>Level</td><td>%Bias</td><td>%CV</td><td>%TE</td></tr>
<tr><td>5.2</td><td>-1.98</td><td>2.07</td><td>6.0</td></tr>
<tr><td>6.5</td><td>-1.45</td><td>1.7</td><td>4.7</td></tr>
<tr><td>8.0</td><td>-1.06</td><td>2.1</td><td>5.1</td></tr>
</table>
</td><td>
Fingerstick whole blood:
<table>
<tr><td>Level</td><td>%Bias</td><td>%CV</td><td>%TE</td></tr>
<tr><td>5.0</td><td>-0.335</td><td>1.90</td><td>4.05</td></tr>
<tr><td>6.5</td><td>-0.334</td><td>1.40</td><td>3.07</td></tr>
<tr><td>8.0</td><td>-0.334</td><td>1.33</td><td>2.94</td></tr>
<tr><td>12.0</td><td>-0.333</td><td>0.55</td><td>1.41</td></tr>
</table>
Venous whole blood:
<table>
<tr><td>Level</td><td>%Bias</td><td>%CV</td><td>%TE</td></tr>
<tr><td>5.0</td><td>0.195</td><td>1.45</td><td>3.04</td></tr>
<tr><td>6.5</td><td>-0.052</td><td>1.27</td><td>2.53</td></tr>
<tr><td>8.0</td><td>-0.206</td><td>1.16</td><td>2.48</td></tr>
<tr><td>12.0</td><td>-0.429</td><td>0.98</td><td>2.35</td></tr>
</table>
</td></tr>
<tr><td>Interference from Hb variants</td><td>
<table>
<tr><td rowspan="2">Variant</td><td rowspan="2">%Variant</td><td colspan="2">Relative bias from reference method</td></tr>
<tr><td>~6.0%</td><td>~9.0%</td></tr>
<tr><td>C</td><td>31-42</td><td>-3.07</td><td>-0.35</td></tr>
<tr><td>S</td><td>33-44</td><td>2.17</td><td>3.42</td></tr>
<tr><td>E</td><td>27-33</td><td>-1.58</td><td>3.46</td></tr>
<tr><td>D</td><td>34-42</td><td>-2.30</td><td>3.35</td></tr>
<tr><td>A2</td><td>4-7</td><td>-5.73</td><td>-4.12</td></tr>
<tr><td>F</td><td>2-28</td><td colspan="2">Bias exceeds -7% when HbF exceeds 7%</td></tr>
</table>
</td><td>
<table>
<tr><td rowspan="2">Variant</td><td rowspan="2">%Variant</td><td colspan="2">Relative bias from reference method</td></tr>
<tr><td>~6.5%</td><td>~8.5%</td></tr>
<tr><td>C</td><td>31-36</td><td>-5</td><td>-2</td></tr>
<tr><td>S</td><td>37-42</td><td>-4</td><td>-1</td></tr>
<tr><td>E</td><td>17-26</td><td>4</td><td>4</td></tr>
<tr><td>D</td><td>39-42</td><td>-2</td><td>-3</td></tr>
<tr><td>A2</td><td>4-6</td><td>-3</td><td>-3</td></tr>
<tr><td>F</td><td>2-32</td><td colspan="2">Bias exceeds -7% when HbF exceeds 7%</td></tr>
</table>
</td></tr>
</table>

5.2 CLIA Test Categorization

As noted above, the Afinion HbA1c Dx test is intended as a CLIA moderate complexity test pursuant to the CLIA regulations (42 C.F.R. Part 493). CLIA was enacted to establish quality standards for laboratory testing to ensure the accuracy, reliability and timeliness of patient test results, regardless of where the test is performed[c]. FDA is responsible for categorizing in vitro diagnostic tests into one of three groups – high complexity, moderate complexity or waived in accordance with the CLIA regulations (42 C.F.R. 493.5). Tests that are not determined to be waived tests are categorized as either moderate complexity or high complexity in accordance with the following seven criteria set forth in the CLIA regulations (42 C.F.R. 493.17):

1. Knowledge required
2. Training and experience required

[c] https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html

3. Reagents and materials preparation required

4. Characteristics of operational steps (e.g., automated or not)

5. Availability and stability of QC, calibration and proficiency testing materials

6. Test system troubleshooting and equipment maintenance

7. Amount/degree of interpretation and judgment required (e.g., to perform pre-analytic, analytic and post-analytic processes to perform resolution of problems)

FDA evaluates and grades tests for level of complexity by assigning scores of 1, 2, or 3 for each of the seven criteria. A score of "1" indicates the lowest level of complexity, and a score of "3" indicates the highest level. The scores are totaled. Test systems receiving total scores of 12 or less are categorized as moderately complex. Test systems, assays or examinations receiving scores above 12 are categorized as high complexity.

CLIA waived tests are defined as those that involve simple laboratory examinations and procedures which employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible or pose no reasonable risk of harm to the patient if the test is performed incorrectly (42 C.F.R. 493.15(b)(2-3)). Tests may be categorized as waived by regulation, by application, or automatically by being designated for over-the-counter use.

5.3 CLIA Laboratory Requirements

Laboratories performing moderate or high complexity tests (non-waived) are subject to specific laboratory standards governing certification, such as: personnel qualification (education and experience) requirements, proficiency testing, patient test management, quality assessment, quality control, and regular inspections by CMS or a CMS-recognized accrediting organization (42 C.F.R. 493.20 and 42 C.F.R. 493.25). Laboratories apply for and receive certificates of compliance or certificates of accreditation if they meet the applicable requirements.

Proficiency testing involves the purchasing of value assigned samples from a CMS accredited proficiency program provider (e.g., College of American Pathology (CAP)). The assigned value of the samples is unknown to the participating laboratory. After purchasing and receiving these samples, typically three to five fresh whole blood samples two to three times a year, the laboratory will run these samples on their testing method and report back the results to the proficiency program provider. The laboratory

will then receive information about how close its results were to the assigned values. Aggregate results from all participating laboratories are then published.

Laboratories conducting only tests categorized as waived are subject to fewer requirements. Such laboratories must follow the manufacturer's instructions for use for a test and must permit inspections by CMS or its agents (42 C.F.R. 493.15(e)(1-2)). Such inspections generally occur only in response to complaints. Some examples of waived tests are: glucose, PT-INR coagulation monitoring, pregnancy tests and lipid panels.

5.4 Point-Of-Care Testing

As shown in **Table 5.4-1** below, POC testing[d] refers to medical diagnostic testing at or near the time and place of patient care. POC testing is not defined by the complexity of the testing and is therefore independent of CLIA categorization. POC testing may occur at sites conducting only waived testing, such as small physician office laboratories, pharmacies, or medical clinics that hold certificates of waiver. Alternatively, POC testing may occur at facilities holding certificates of compliance or accreditation to conduct moderate or high complexity testing, such as large physician group practices or hospital satellite laboratories.

Regardless of facility type, POC testing provides a rapid, convenient alternative to referring a patient to a central laboratory for diagnostic evaluation. When testing is performed away from the POC, it can take hours or days before a clinician receives the results and is able to review them in the clinical context of overall patient presentation. In contrast, when testing is performed at the POC, clinicians have rapid results that can be considered at the time of clinical consultation. This allows for more timely decision making and enhanced communication with the patient. For example, POC HbA1c testing has been shown to result in more rapid intensification of therapy in those with diabetes and as a result, significantly better glycemic control.[14-22] The ADA recommends the use of POC HbA1c testing for monitoring patients with diabetes, and this practice has been widely adopted.[23]

[d] CDC defines "point-of-care testing" as "a phrase used to describe the location where testing is performed, such as at the bedside or near the site of patient care. While some point-of-care tests are approved for a CLIA waiver, advances in technology that enhance the rapidity of testing are allowing more complex, non-waived testing to be performed at or near the site of patient care." http://wwwn.cdc.gov/clia/resources/testcomplexities.aspx

Table 5.4-1: CLIA Laboratory Requirements

Certification	Test Complexity	CLIA Requirements	Laboratory Types
Certificate of Waiver	Waived testing	Follow manufacturer's instruction for use for the CLIA-waived tests conducted in the lab Permit inspections by CMS (usually only in cases of complaints)	POC sites including: • Small physician office lab • Pharmacies • Health fairs • Nursing homes • Coagulation clinics • Employee health screening • Other clinics
Certificate of Accreditation or Compliance	Non-waived testing (high and moderate complexity)	Facility administration Personnel qualifications and training General laboratory systems Patient test management Quality control Proficiency testing[e] Quality assessment Permit inspections	Clinical labs Centralized hospital lab POC sites* that may include: • large physician group or clinic • hospital satellite lab • ED or ICU

*Would typically conduct moderate, not high complexity testing due to general size of high complexity testing systems

[e] Per CLIA regulations, the laboratory is required to enroll in a proficiency testing program approved by CMS, testing the survey samples in the same manner as patients' specimens (42 CFR 493.801). The frequency and number of samples may vary by test specialty. Unsatisfactory performance can result in suspension of testing.

6. FEEDBACK AND DISCUSSION

In this panel meeting, FDA is soliciting feedback on Alere's 510(k) premarket notification for the Alere Afinion HbA1c Dx test. Alere's perspectives on topics the company expects the panel to be asked to consider are presented below.

Use of the Afinion HbA1c Dx test for the Diagnosis of Diabetes in Moderate Complexity POC Settings

Quality assurance and proficiency testing have been raised by the ADA statements and from discussion with our advisors as important considerations to be addressed in the use of POC HbA1c diagnostic testing. In July 2009, an international expert committee with members appointed by the ADA, the European Association for the Study of Diabetes, and the International Diabetes Federation published a report on the role of HbA1c testing for the diagnosis of diabetes.[24]. In that paper, the following statement appears:

"Point-of-care instruments have not yet been shown to be sufficiently accurate or precise for diagnosing diabetes."

When the ADA subsequently published standards of care in 2010, the recommendations from the international expert committee paper were adopted, including the statement regarding POC assays. This statement persists within the current ADA standards of care despite the long standing recommendation to implement POC HbA1c testing in the monitoring of diabetes within these same standards of care. Over time, the reference to POC testing for diagnostic use has evolved as follows.

*Standards of Medical Care in Diabetes **2010**[25]:*

- *"Point-of Care A1c assays are **not sufficiently accurate at this time** to use for diagnostic purposes."*

*Standards of Medical Care in Diabetes **2016**[2]:*

- *"Although point-of-care A1C assays may be NGSP certified, proficiency testing is not mandated for performing the test, so use of point-of-care assays for diagnostic purposes is not recommended."*

To better understand the intent, the origin, and evolution of these statements, Alere interviewed leading experts in the field of diabetes, many of whom have held high ranking positions within the ADA and have participated in the development of ADA or

international standards. Among those experts that Alere has interviewed on this matter are:

Advisor Name	Affiliations	Experience
Dr. Vivian Fonseca, MD, FRCP	• Tullis-Tulane Alumni Chair in Diabetes • Chief, Section of Endocrinology	• Past President, Medicine & Science ADA • Editor-in-chief of the Journal of Diabetes Complications
Dr. Robert Henry, MD	• Chief, Section of Endocrinology, Metabolism & Diabetes Veterans Affairs Healthcare System, San Diego • Chief, Center for Metabolic Research	• 2011 President, Medicine & Science ADA
Dr. Silvio Inzucchi, MD	• Professor of Medicine (Endocrinology) , Yale University • Clinical Director, Section of Endocrinology • Director, Yale Diabetes Center	• Lead author on the position paper of the ADA and EASD joint task force on the Management of Hyperglycemia in Type 2 Diabetes. • Reviewer and consultant for the 2015 and 2016 ADA Standards of Care in Diabetes
Dr. Richard Kahn, PhD	• Clinical Professor of Medicine, University of North Carolina at Chapel Hill	• Past Chief Scientific & Medical Officer of the ADA • Member of the International Expert Panel Publication on HbA1c for Diagnosis
Dr. Randie Little, PhD	• Dept. of Pathology & Anatomical Sciences, University of Missouri School of Medicine	• (National Glycohemoglobin Standardization Program) NGSP Network Coordinator • Co-Director of Diabetes Diagnostic Laboratory • Member of IFCC Integrated Project on HbA1c
Dr. David Nathan, MD	• Professor of Medicine, Harvard Medical School • Physician, Massachusetts General Hospital	• Architect of DCCT trial and co-chair of continuing DCCT/EDIC trial • Chair, 2009 Intl Expert Committee on HbA1c for Diagnosis • Chair of NIH Diabetes Prevention Program (DPP) • 2015 ADA award winner for "outstanding Achievement in Clinical Diabetes
Dr. Julio Rosenstock, MD	• Director of the Dallas Diabetes and Endocrine Center • Clinical Professor of Medicine at the University of Texas Southwestern	• Current Associate Editor of Diabetes Care (the journal that publishes the ADA Professional Practice Standards of Care)

Advisor Name	Affiliations	Experience
	Medical School at Dallas	
Dr. David Sacks, MD, MB, ChB, FRCPath, FACB	• Chief, Clinical Chemistry Service, NIH Clinical Center Department of Laboratory Medicine	• Chair of NGSP Steering Committee • Oversees HbA1c CAP proficiency testing program
Dr. Mitchell Scott, PhD	• Professor, Pathology and Immunology at the Washington University School of Medicine • Medical Co-Director, Clinical Chemistry	• Past President of AACC, ACLPS, ABCC • Associate Editor, Clinical Cheistry • CLSI – subcommittees for QC based risk management, POC BG, and Vice Chair for Eval protocols,

The key learnings that Alere took away from these expert consultations were that:

- The International Expert Committee chose to make the original statement in 2009 because the adoption of HbA1c for diagnostic use was a major policy change, but little was known about the accuracy of POC devices for HbA1c testing at the time.
- The 2010 ADA statement on the use of POC devices for diagnostic testing was as a carry-over from the International Expert Committee's 2009 paper.
- The 2016 ADA statement does not differentiate moderately complex POC HbA1c use (which does require proficiency testing) from CLIA waived POC HbA1c use (which does not require proficiency testing). This most recent ADA statement does not apply to the current Alere submission for clearance of a moderately complex test, because proficiency testing would be required with such a clearance.
- The ADA virtually always follows the recommendations of the FDA and would very likely revise its current statement once a POC HbA1c method is FDA cleared. The ADA's practice, since the inception of its Standards of Medical Care in 1989, has been not to recommend the use of a drug or device that has not been FDA approved, nor to make a recommendation that is in conflict with FDA approvals.
- Clearance should be based on analytical performance and safety (the origin of doubt in the ADA statement) and not on the treatment setting where the testing is performed.

Separation of the CLIA Waived and Moderate Complexity Afinion HbA1c Test Systems

Alere has provided additional clarification to the FDA on our proposed system design to ensure that moderate complexity Afinion HbA1c Dx tests cannot be used on the CLIA waived Afinion instruments. Although the Afinion instrument and HbA1c test cartridge for monitoring and for diagnostic use have the same technological characteristics, at clearance of the moderate complexity Afinion HbA1c Dx test the proposed mitigations would go into place:

- There would be two instrument configurations in the market. One for only CLIA waived tests and one for all tests including moderately complex HbA1c. The CLIA waived configured instruments could not report results for the moderately complex Afinion HbA1c Dx test cartridges. These different instrument configurations would have:
    - Different part numbers (ordering or catalogue numbers)
    - Different descriptions noting distinctions for CLIA waiver or moderate complexity use
- There would be two different HbA1c test cartridges: one for CLIA waived monitoring use only and another one for moderate complexity diagnostic use. These would have:
    - Different product names
    - Different part numbers (ordering or catalogue numbers)
    - Different descriptions noting distinctions for CLIA waiver or moderate complexity use
    - Different package inserts noting intended use and CLIA statements
    - Different packaging noting different product name and intended use

The proposed design of the two Alere Afinion systems will reduce the risk of a CLIA waived laboratory using non-CLIA waived Afinion assays. The probability that a CLIA waived laboratory will order and use the moderate complexity Alere Afinion HbA1c Dx system (assay and analyzer) for the diagnosis of diabetes or identification of patients at risk of developing diabetes as well as the other cleared moderate complexity Afinion assays is considered to be very low with this design. Customers are informed of CLIA categorization of the test systems in all labeling as well as during order processing.

Alere has reviewed and solicited input regarding the system design for separation of the moderate complexity test from the CLIA waived test. Alere has heard that this solution seems to provide clear separation of the moderate complexity and CLIA waived versions of the test systems for those intending to use the products as labeled for their indications for use.

Considerations for an Afinion HbA1c Dx CLIA Waiver

As noted previously, CLIA waived tests are defined as those that involve simple laboratory examinations and procedures which employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible or pose no reasonable risk of harm to the patient if the test is performed incorrectly (42 CFR 493.15(b)(2-3)). There are three ways in which a test can be categorized as CLIA waived:

7. By regulation **(**eg, dipstick or tablet reagent urinalysis (non-automated) for various analytes; urine pregnancy tests; ovulation tests; (21 CFR 493.15(c)); or
8. Cleared by FDA for home use (21 CFR 493.15(b)(1)); or
9. Meet the statutory criteria for waiver. This requires FDA approval via application utilizing criteria outlined in 2008 FDA guidance: *Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices (January 30, 2008).*

Since the Afinion HbA1c Dx test is neither waived by regulation nor cleared for home use, in order for Alere to market the Afinion HbA1c Dx test as a waived test, Alere would first need to gain FDA clearance as a moderate complexity test and then submit a subsequent application for CLIA waiver. Such an application would need to establish that the test meets the requirements for CLIA waiver. Under FDA's 2008 guidance, such an application would include at least the following:

- A clinical accuracy study at a minimum of three CLIA waived sites and with blood samples collected from a minimum of 360 subjects. Accuracy would be demonstrated by comparing the Afinion HbA1c Dx test to a suitable selected comparative method using an error grid agreed upon with FDA in advance of conducting the study. The error grid would consist of an Allowable Total Error (ATE) zone within which 95% of the results by the waived method must fall. The

error grid would also consist of Limits of Erroneous Results (LER) zones in which no results may fall.

- A risk analysis to identify sources of error and flex studies to demonstrate robust design. Flex studies and results would have to support the ability of the control measures to detect and mitigate any potential testing errors.
- Verification and validation of control measures at operational limits.

Prior to the initiation of validation studies for the Afinion HbA1c Dx test CLIA waiver application, Alere will use the pre-submission process in order to receive FDA's full review of and feedback on its study protocols.

Conclusion

As described above, the available data and information establish the safety, effectiveness, and performance of the proposed moderate complexity Afinion HbA1c Dx test and its substantial equivalence to the predicate device (the Cobas C501 Tina-Quant HbA1cDx Gen.3 assay (k121610)). Historical concerns about the lack of data for POC HbA1c tests are not applicable to Alere's pending submission given the extensive data available for the Alere test, concerns about lack of proficiency testing are not relevant to the current submission for a CLIA moderate complexity test, and Alere has established multiple means for avoiding off-label use of the Afinion HbA1c Dx test in CLIA waived environments. A CLIA waiver for the test would require a future application, meeting all FDA criteria.

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510(k) SUMMARY FOR ALERE AFINION™ HbA1c Dx

A 510(k) Summary provides a high-level discussion of the content of a 510(k) and includes all of the elements identified in 21 CFR §807.92. The 510(k) Summary must contain sufficient detail to provide an understanding of the basis for a determination of substantial equivalence. FDA verifies the accuracy and completeness of the information included in the 510(k) Summary and if the product is cleared for marketing, posts this information on the FDA website.

The following 510(k) Summary was prepared in accordance with 21 CFR §807.92 and included in the premarket notification (k153726) for the Alere Afinion™ HbA1cDx.

510(k) SUMMARY

GENERAL INFORMATION

Applicant Name: Alere Technologies AS
Kjelsaasveien 161
PO Box 6863 Rodeloekka
NO-0504 Oslo
Norway
Establishment #9613069

Company Contact: Dawn Allenby
Associate Director, Regulatory Affairs
Phone: (858) 805-2154
Email: dawn.allenby@alere.com

Date Prepared: December 23, 2015

DEVICE IDENTIFICATION

Trade or Proprietary Names:	Alere Afinion™ HbA1c Dx
Common Name:	Afinion™ HbA1c Dx test Device Classification
Name:	Hemoglobin A1c Test
System Product Codes:	PDJ
Regulatory Class:	Class II (Special Controls) Classification Regulation: 21 CFR 862.1373
Predicate Device:	Cobas C501 Tina-Quant HbA1cDx Gen.3 assay (k121610)

DEVICE DESCRIPTION

The Alere Afinion™ HbA1c Dx is a fully automated boronate affinity assay for the determination of the percentage of hemoglobin A1c in human whole blood. The Alere Afinion™ HbA1c Dx is a modification of the existing device, Alere Afinion™ HbA1c for use with the Alere Afinion™ AS100 Analyzer and Alere Afinion™ HbA1c Controls, with the addition of a diagnostic intended use.

The test begins with a blood sample collected with the integrated sampling device before the test cartridge is placed in the cartridge chamber of the Alere Afinion™ AS100 Analyzer. The sample is then automatically diluted and mixed with a solution that releases hemoglobin from the erythrocytes. After the hemoglobin is precipitated, the sample mixture is transferred to a blue boronic acid conjugate which binds to the cis-diols of glycated hemoglobin. This reaction mixture is soaked through a filter membrane and all precipitated hemoglobin, conjugate-bound and unbound (i.e. glycated and non- glycated hemoglobin) remains on the membrane. Excess conjugate is removed with a washing reagent. The analyzer measures the reflectance of the precipitate on the membrane as blue (glycated hemoglobin) and red (total hemoglobin) color intensities. The analyzer calculates a ratio proportional to the percentage of HbA1c in the sample and displays as the % HbA1c (NGSP).

INTENDED USE

Alere Afinion™ HbA1c Dx is an *in vitro* diagnostic test for quantitative determination of glycated hemoglobin (% hemoglobin A1c, HbA1c) in human whole blood.

This test is to be used as an aid in the diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.

The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.

For use in clinical laboratories and point of care laboratory settings.

COMPARISON WITH PREDICATE

Attribute	Predicate Device Cobas C501 Tina-Quant HbA1cDx Gen.3 assay (k121610)	Candidate Device Alere Afinion™ HbA1c Dx
Similarities		
Intended Use	Quantitative determination of hemoglobin A1c for the diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes	Same
User environment	For use by health care professionals in clinical laboratories	Same
Sample types	Anticoagulated venous or capillary blood	Same
Anticoagulants	Li-Heparin, K2-EDTA, K3-EDTA, KF/Na2- EDTA, Na-Heparin, NaF/K-Oxalate and NaF/Na2-EDTA	Same
Units of measurement	% HbA1c (DCCT/NGSP)	Same
Storage requirements	2-8°C until expiration date	Same
Controls	Provided by manufacturer	Same
Standardization	Traceable to the International Federation of Clinical Chemisty and Laboratory Medicine (IFCC) and Diabetes Control and Complications Trial (DCTT) reference method. Certified via the National Glycohemoglobin Standardization Program (NGSP).	Same

Attribute	Predicate Device Cobas C501 Tina-Quant HbA1cDx Gen.3 assay (k121610)	Candidate Device Alere Afinion™ HbA1c Dx
	Similarities, continued	
Expected values	**Protocol 1 (IFCC)** 20-42 mmol/mol HbA1c **Protocol 2 (DCCT/NGSP)** 4.0 – 6.0 %HbA1c	**DCCT/NGSP** 4.0 – 6.0 %HbA1c
	Differences	
Assay principle	HbA1c determination by turbidimetric inhibition immunoassay method. Hemoglobin determination by converting to a derivative with a characteristic absorption spectrum which is measured bi- chromatically.	Boronate affinity assay. Hemoglobin determination by reflectance measurements of blue conjugate of glycated hemoglobin and red total hemoglobin.
Hardware	Cobas c501	Alere Afinion™ AS100 Analyzer
Calibrators	Provided by manufacturer	Calibration by user no required; factory calibrated
Reporting range	4.2–20.1 % HbA1c	4.00–15.00 % HbA1c

PERFORMANCE CHARACTERISTICS

1) Precision/Reproducibility

Precision - Internal

The precision of the Alere Afinion™ HbA1c Dx was evaluated based on CLSI guideline EP05-A2. Four levels of HbA1c in anticoagulated venous whole blood patient samples at the following targeted HbA1c values: 5, 6.5, 8 and 12 %HbA1c, were utilized in the study. The tcontrols, Alere Afinion™ HbA1c Control CI and CII, and three test cartridge lots were included in the study. Four replicates of venous whole blood and the two controls were tested twice a day for ten days with each of the three lots. Different analyzers were used, one for each of the three test cartridge lots.

Table 1: Internal precision

Level	Lot	Mean %HbA1c	Repeatability		Between day		Between run		Within device (Total)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low	1	5.16	0.05	0.9	0.01	0.1	0.00	0.0	0.0	0.9
	2	5.08	0.04	0.8	0.01	0.3	0.00	0.0	0.0	0.9
	3	5.03	0.05	1.1	0.02	0.4	0.00	0.0	0.0	1.1
Threshold	1	6.47	0.07	1.0	0.02	0.4	0.00	0.0	0.0	1.1
	2	6.38	0.06	1.0	0.00	0.0	0.01	0.1	0.0	1.0
	3	6.37	0.05	0.8	0.02	0.3	0.00	0.0	0.0	0.9
Medium	1	8.42	0.08	1.0	0.02	0.2	0.00	0.0	0.0	1.0
	2	8.37	0.09	1.1	0.00	0.0	0.01	0.1	0.0	1.1
	3	8.37	0.07	0.8	0.03	0.4	0.00	0.0	0.0	0.9
High	1	11.82	0.11	0.9	0.05	0.4	0.00	0.0	0.1	1.0
	2	11.81	0.10	0.8	0.01	0.1	0.00	0.0	0.1	0.9
	3	11.78	0.14	1.2	0.00	0.0	0.00	0.0	0.1	1.2
Control CI	1	6.34	0.05	0.8	0.00	0.0	0.00	0.0	0.0	0.8
	2	6.11	0.05	0.9	0.00	0.0	0.00	0.0	0.0	0.9
	3	6.15	0.04	0.7	0.02	0.4	0.00	0.0	0.0	0.8
Control CII	1	8.34	0.08	0.9	0.01	0.2	0.00	0.0	0.0	0.9
	2	8.49	0.06	0.7	0.00	0.0	0.00	0.0	0.0	0.7
	3	8.35	0.06	0.7	0.00	0.0	0.02	0.2	0.0	0.7

Precision – External

The precision of the Alere Afinion™ HbA1c Dx was evaluated externally. Four levels of HbA1c in anticoagulated venous whole blood patient samples at the following targeted HbA1c values: 5, 6.5, 8 and 12 %HbA1c, were evaluated at each of three study sites. Two controls, Alere Afinion™ HbA1c Controls CI and CII, and three test cartridge lots were included in the study. Four replicates of venous whole blood and the two controls were analyzed twice a day for ten days with each of the three lots at each of the three sites.

Table 2: External precision - results from site 1

	Mean	Repeatability		Between		Between day		Between lot		Total	
Level	%HbA1c	SD	%CV	S	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.08	0.061	1.20	0.0	0.00	0.000	0.00	0.034	0.67	0.070	1.38
Threshol	6.44	0.080	1.24	0.0	0.20	0.000	0.00	0.042	0.65	0.091	1.41
Medium	8.48	0.101	1.19	0.0	0.00	0.000	0.00	0.029	0.34	0.105	1.24
High	12.11	0.140	1.16	0.0	0.00	0.000	0.00	0.000	0.00	0.140	1.16
C I	6.35	0.052	0.82	0.0	0.00	0.017	0.27	0.024	0.38	0.060	0.95
C II	8.51	0.063	0.74	0.0	0.00	0.010	0.12	0.000	0.00	0.064	0.75

Table 3: External precision - results from site 2

	Mean	Repeatability		Between		Between day		Between lot		Total	
Level	%HbA1c	SD	%CV	S	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.24	0.073	1.39	0.0	0.34	0.000	0.00	0.030	0.57	0.081	1.55
Threshol	6.18	0.061	0.99	0.0	0.00	0.000	0.00	0.047	0.76	0.077	1.25
Medium	7.90	0.082	1.04	0.0	0.00	0.005	0.06	0.041	0.52	0.092	1.16
High	12.36	0.101	0.82	0.0	0.24	0.000	0.00	0.000	0.00	0.105	0.85
C I	6.31	0.063	1.00	0.0	0.00	0.000	0.00	0.018	0.29	0.066	1.05
C II	8.45	0.068	0.80	0.0	0.00	0.000	0.00	0.000	0.00	0.068	0.80

Table 4: External precision - results from site 3

	Mean	Repeatability		Between		Between day		Between lot		Total	
Level	%HbA1c	SD	%CV	S	%CV	SD	%CV	SD	%CV	SD	%CV
Low	4.74	0.048	1.01	0.0	0.00	0.011	0.23	0.045	0.95	0.067	1.41
Threshol	6.62	0.073	1.10	0.0	0.00	0.011	0.17	0.000	0.00	0.074	1.12
Medium	8.15	0.088	1.08	0.0	0.00	0.000	0.00	0.000	0.00	0.088	1.08
High	11.81	0.108	0.92	0.0	0.00	0.000	0.00	0.000	0.00	0.108	0.92
C I	6.31	0.052	0.82	0.0	0.00	0.000	0.00	0.000	0.00	0.052	0.82
C II	8.46	0.069	0.82	0.0	0.00	0.000	0.00	0.000	0.00	0.069	0.82

Table 5: External precision - combined results (Root Mean Squared SD and %CV)

Level	Mean	Repeatability		Between		Between day		Between lot		Total	
	%HbA1c	SD	%CV	S	%CV	SD	%CV	SD	%CV	SD	%CV
Low	5.02	0.061	1.21	0.0	0.20	0.007	0.13	0.038	0.75	0.073	1.45
Threshol	6.41	0.072	1.12	0.0	0.12	0.006	0.10	0.037	0.58	0.081	1.27
Medium	8.18	0.090	1.11	0.0	0.00	0.003	0.04	0.029	0.36	0.095	1.16
High	12.09	0.118	0.97	0.0	0.14	0.000	0.00	0.000	0.00	0.119	0.98
C I	6.32	0.056	0.89	0.0	0.00	0.010	0.16	0.017	0.27	0.060	0.94
C II	8.48	0.067	0.79	0.0	0.00	0.006	0.07	0.000	0.00	0.067	0.79

Between-instrument precision

Between-instrument precision of the Alere Afinion™ HbA1c Dx was evaluated using 14 Alere Afinion™ AS100 Analyzers. Four whole blood samples were measured in six replicates on each analyzer with one test cartridge lot for a total of 84 replicates per sample.

Table 6: Between-instrument results

Level	Mean %HbA1c	Between instrument	Between instrument CV
Low	5.46	0.04	0.7
Low	5.47	0.05	0.9
Threshold	6.54	0.05	0.8
Medium	8.85	0.09	1.0

Lot-to-lot variation

The lot-to-lot variation for the Alere Afinion™ HbA1c Dx assay was evaluated using three manufacturing lots of test cartridges and 18 EDTA whole blood samples spanning the assay measuring (reportable) range. Each sample was analysed in one replicate with each test cartridge lot on the same Alere Afinion™ AS100 Analyzer. The results from test cartridge lots were compared pairwise using Bland-Altman analysis.

Table 7: Lot-to-lot variation results

Comparison	Relative Bias (%)	95% Limit of Agreement
Lot 3 - Lot 1	0.08	-3.5 to 3.7
Lot 2 - Lot 1	-0.17	-4.0 to 3.6
Lot 3 - Lot 2	0.25	-4.4 to 4.9

2) Method Comparison

The method comparison study was performed using an NGSP secondary reference laboratory method (Tosoh Glycohemoglobin test on the G8 HPLC analyzer) as the comparator (reference) method. Three production lots of Alere Afinion™ HbA1c Dx test cartridges were evaluated. Two lots were assigned to each of three study sites. Samples from each study subject were tested with both fingerstick samples and fresh venous EDTA samples in single replicates per lot. A total of 120 subjects were included in the study.

Table 8: Sample distribution

%HbA1c Interval Alere Afinion™ HbA1c Dx	Number of subjects				Total %
	Site 1	Site 2	Site 3	Total	
4.0 – 5.0	2	2	1	5	4.2
5.1 – 6.0	5	5	5	15	12.5
6.1 – 6.5	10	10	10	30	25.0
6.6 – 7.0	12	8	10	30	25.0
7.1 – 8.0	7	6	7	20	16.7
8.1 – 9.0	3	4	3	10	8.3
9.1 – 15.0	3	3	4	10	8.3
Total	42	38	40	120	100.0

Table 9: Weighted Deming regression –combined results from 3 sites and 3 lots

	Fingerstick	Venous whole
Slope	0.997	0.991
Intercept	0.000	0.053
Correlation coefficient ®	0.991	0.990
Number of samples	120	120
Results range Afinion	4.66 to 11.58	4.72 to 11.49

3) Total Error

Using the results of bias estimation (%Bias) from the method comparison study and precision estimates in the precision study from the three study sites, the Total Error (TE) at four concentrations (5.0, 6.5, 8.0 and 12.0 %HbA1c) was calculated. The precision estimates from venous whole blood were used to estimate TE both for fingerstick samples and venous whole blood samples with an acceptable %TE of ≤6.0%.

Table 10: Total error – fingerstick whole blood samples

%HbA1c Level	%Bias	%CV	%TE
5.0	-0.335	1.45	3.16
6.5	-0.334	1.27	2.81
8.0	-0.334	1.16	2.60
12.0	-0.333	0.98	2.25

Table 11: Total error - venous whole blood samples

%HbA1c Level	%Bias	%CV	%TE
5.0	0.195	1.45	3.04
6.5	-0.052	1.27	2.53
8.0	-0.206	1.16	2.48
12.0	-0.429	0.98	2.35

4) Endogenous Interference

Six endogenous substances spiked into whole blood sample pools were evaluated for potential interference of the assay in accordance with CLSI guideline EP7-A2. Two HbA1c levels, one near the medical decision level and one above it, were tested for each endogenous substance. Each sample was tested for %HbA1c with ten replicates on a single Alere Afinion™ AS100 Analyzer, using a single reagent lot. The corresponding non-spiked sample which contained no added substance was tested also with ten replicates. A mean was calculated for each set of ten. Significant interference was defined as exceeding a 7% change in %HbA1c value from the control (non-spiked sample). The results for the spiked samples were compared to the control with no interference at the stated concentrations.

Table 12: Endogenous interference results

Endogenous substance	Test concentration with no significant interference
Bilirubin, conjugated	600 mg/L
Bilirubin, unconjugated	600 mg/L
Glucose	10 000 mg/L
Intralipid	10 000 mg/L
Rheumatoid factor	780 000 IU/L
Total protein	15 g/dL

5) Hemolysis Interference

Potential interference from hemolysis was assessed in accordance with CLSI guideline EP7-A2. Whole blood samples with two HbA1c levels, one near the medical decision level and one above it, were used for the testing. Hemolysis in the blood samples was simulated by spiking with fresh hemolysate prepared from the native samples. Hemolysate was added to the corresponding native sample to volume percentages of 5, 10, 15 and 20%. The exact degree of hemolysis was measured in each spiked fraction. Each spiked sample and corresponding non-spiked sample was tested in ten replicates on a single Alere Afinion™ AS100 analyzer using one test cartridge lot. The mean result from the manipulated sample was compared to the mean result from the corresponding native control sample. Significant interference was defined as exceeding a 7% change in %HvA1c value from the control (native sample). The results demonstrated no interference up to 14% hemolysis.

6) Drug Interference

Twenty drugs spiked into whole blood sample pools were tested for potential interference with the assay in accordance with CLSI guideline EP7-A2. The drug substances included commonly used antibiotics, analgesic agents, immunosupressants, anti-inflammatory drugs, anticoagulants and prescription drugs for diabetes treatment. Two HbA1c levels, one near the medical decision level and one above it, were tested for each endogenous substance. Each spiked sample was tested for %HbA1c in ten replicates on a single Alere Afinion AS10 Analyzer, using a single reagent lot. The corresponding non-spiked sample which contained no added substance was tested also with ten replicates. A mean was calculated for each set of ten. Significant interference was defined as exceeding a 7% change in %HbA1c value from the control (non-spiked sample). The results for the spiked samples were compared to the control with no interference at the stated concentrations.

Table 13: Drug interference results

Drug substance	Test concentration with no significant interference (mg/L)
Acetaminophen	200
Acetylcysteine	1663
Ascorbic	300
Cefoxiti	2500
Metformi	40
Methyldop	20
Cyclosporine C	5
Glyburid	1.9
Metronidazole	200
Ampicilli	1000
Acetylsalicylic acid	1000
Doxycyclin	50
Ibuprofe	500
Cyclosporine A	5
Levodop	20
Hepari	5000 U/L
Salicylic	599
Theophyllin	100
Phenylbutazone	400
Rifampici	64

7) Cross reactivity with Hemoglobin Derivatives

Interference effects from hemoglobin derivatives were assessed. Whole blood samples with two HbA1c levels, one near the medical decision level and one above it, were used for the testing. For each HbA1c level, two whole blood pools were prepared for each derivative, one without derivative (control) and one with high concentration of derivative. Each sample was tested in ten replicates on a single Alere Afinion™ AS100 Analyzer using one test cartridge lot. A mean was calculated for each set of ten. Significant interference was defined as exceeding a 7% change in %HbA1c value from the control (non-spiked sample). The results for the spiked samples were compared to the control with no interference at the stated concentrations.

Table 14: Cross reactivity with hemoglobin derivatives results

Hemoglobin derivative	Test concentration with no significant interference
Acetylated hemoglobin	4.6
Carbamylated hemoglobin	13.8
Labile	11.4
Glycated albumin	7.7

8) Hemoglobin Variants Interference

A hemoglobin variant interference study was performed based on CLSI guideline EP7-A2. A total of 151 fresh EDTA whole blood samples that contained one of six common hemoglobin variants were included in the study. All samples were tested with Alere Afinion™ HbA1c Dx and with an NGSP reference method that is known to be free from the hemoglobin interference being tested. The level of Hb variant was determined by the Capillarys 2 Flex Piercing method. Interference effect was assessed by comparing the results from Alere Afinion HbA1c Dx to the reference method result for samples with potentially interfering hemoglobin variants. Significant interference was defined as exceeding a 7% change in %HbA1c value from the reference method. Table 13 indicates the number, range and concentration of samples and Table 14, results from the study.

Table 15: Sample profile for hemoglobin variant study

Hemoglobin Variant	Number of samples	Range of % content of variant	Range of concentration in %Hb
HbA2	20	4-6	5.8-
HbS	20	37-42	5.6-
HbC	20	31-36	5.5-
HbE	20	17-26	6.1-
HbD	20	39-42	6.1-
HbF	51	2-32	6.2-

Table 16: Hemoglobin variant results

Hemoglobin Variant	Percent relative bias from reference method at two levels of the HbA1c samples	
	Level 1: ~6.5 %HbA1c	Level 1: ~8.5 %HbA1c
HbA2	-3	-3
HbS	-4	-1
HbC	-5	-2
HbE	4	4
HbD	-2	-3
HbF	Bias exceeds -7% when amount of HbF in the sample exceeds	

^ A negative bias with HbF is independent of %HbA1c level but proportional to the %HbF content.

No significant interference was observed for the HbA2, HbS, HbC, HbE and HbD. For HbF interference, the device includes the following prominent boxed warning:

> This device has significant negative interference with fetal hemoglobin (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF including those with known Heredity Persistence of Fetal Hemoglobin. Refer to the Analytical specificity and Limitations sections in this package insert for details.

9) Linearity

The linearity of the Alere Afinion™ HbA1c assay was previously established in k050574, and was not re-established for the additional indications for use for the Afinion™ HbA1c Dx assay. The reportable range for this device is 4.00-15.00 % HbA1c (DCCT/NGSP).

CONCLUSION

The information and data in this 510(k) application demonstrate that the Alere Afinion™ HbA1c Dx assay as performed on the Alere Afinion AS10 Analyzer is an accurate and precise test that correlates well with current cleared methods and NGSP standardized testing for the quantitation of HbA1c. Performance criteria as outlined in the special control requirements of 21 CFR 862.1373 for the diagnosis of diabetes have been met. Based on the criteria stated above, this device is found to be substantially equivalent to the predicate device.

PROPOSED LABELING

1. Alere Afinion™ HbA1c Dx Package Insert
2. Alere Afinion™ HbA1c Dx Quick Guide
3. Alere Afinion™ AS100 Analyzer User Manual

1

Alere Afinion™

HbA1c Dx

Hemoglobin A1c test
For use with the Alere Afinion™ AS100 Analyzer

Please consult the Alere Afinion™ AS100 Analyzer User Manual for information related to the general operation of the Analyzer and Alere Afinion™ Test Cartridge handling.

Caution!
Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

Technical Support
The manufacturer provides a toll free line for technical support. Call 1-866-216-9505. The toll free number is available for use only in the United States of America.

REF XXXXXX

XXXXXXX Rev. XXXX/XX

Alere Afinion™ HbA1c Dx

For use with the Alere Afinion™ AS100 Analyzer.

This device has significant negative interference with fetal hemoglobin (HbF). HbA1c results are invalid for patients with abnormal amounts of HbF including those with known Heredity Persistence of Fetal Hemoglobin. Refer to the Analytical specificity and Limitations sections in this package insert for details.

CLIA statement

Alere Afinion™ HbA1c Dx is categorized as a moderately complex assay under the Clinical Laboratory Improvement Amendment of 1988 (CLIA`88).

PRODUCT DESCRIPTION

Intended use

Alere Afinion™ HbA1c Dx is an in vitro diagnostic test for quantitative determination of glycated hemoglobin (% hemoglobin A1c, HbA1c) in human whole blood.

This test is to be used as an aid in the diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.

The measurement of % HbA1c is recommended as a marker of long-term metabolic control in persons with diabetes mellitus.

For use in clinical laboratories and point of care laboratory settings.

Summary and explanation of the test

The human erythrocyte is freely permeable to glucose. Within each erythrocyte a slow, continuous, non-enzymatic process between hemoglobin A and various sugars takes place. The product formed is known as glycated hemoglobin, or glycohemoglobin[1].

An International Expert Committee has concluded that measurements of HbA1c can be used to diagnose diabetes mellitus and identify patients that may be of risk of developing diabetes[2].

The chronic elevated blood sugar level of persons with diabetes mellitus will over time cause damage to the small vessels of the body. This damage develops slowly over years and is known to cause late complications. Good metabolic control, i.e. lowering the % HbA1c, has proven to delay the onset and slowing the progression of diabetes late complications[3,4,5].

Principle of the assay

Alere Afinion™ HbA1c Dx is a fully automated boronate affinity assay for the determination of the percentage of hemoglobin A1c in human whole blood.

The Alere Afinion™ HbA1c Dx Test Cartridge contains all of the reagents necessary for the determination of % HbA1c. The sample material is collected with the integrated sampling device before the Test Cartridge is placed in the cartridge chamber of the Alere Afinion™ AS100 Analyzer. The blood sample is then automatically diluted and mixed with a solution that releases hemoglobin from the erythrocytes. The hemoglobin precipitates. This sample mixture is transferred to a blue boronic acid conjugate, which binds to the cis-diols of glycated hemoglobin. This reaction mixture is soaked through a filter membrane and all precipitated hemoglobin, conjugate-bound and unbound (i.e. glycated and non-glycated hemoglobin) remains on the membrane. Any excess of conjugate is removed with a washing reagent.

The Analyzer evaluates the precipitate on the membrane. By measuring the reflectance, the blue (glycated hemoglobin) and the red (total hemoglobin) color intensities are evaluated, the ratio between them being proportional to the percentage of HbA1c in the sample. The % HbA1c is displayed on the Alere Afinion™ AS100 Analyzer.

Standardization

Alere Afinion™ HbA1c Dx is traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Reference Method for Measurement of HbA1c[6,7,8]. HbA1c values are reported according to the National Glycohemoglobin Standardization Program (NGSP) recommendations at DCCT (Diabetes Control and Complications Trial) level[3,7].

Alere Afinion™ HbA1c Dx is certified by NGSP.

Materials provided (contents per 15 tests unit)

15 Test Cartridges packed separately in foil pouches with a desiccant bag.
1 Package Insert

Materials required, but not provided with the kit

- Alere Afinion™ AS100 Analyzer
- Alere Afinion™ AS100 Analyzer User Manual (provided with Alere Afinion™ AS100 Analyzer)
- Alere Afinion™ HbA1c Dx Quick Guide (provided with Alere Afinion™ AS100 Analyzer)
- Alere Afinion™ HbA1c Control
- Standard blood collection equipment

Description of the Alere Afinion™ HbA1c Dx Test Cartridge

The main components of the Test Cartridge are the sampling device (1) and the reaction container (3). The Test Cartridge has a handle (4), a barcode label with lot specific information (5) and an ID area for sample ID (7). See Figure 1 below.

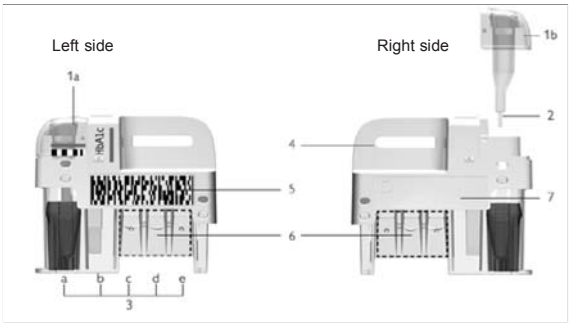


Figure 1 Alere Afinion™ HbA1c Dx Test Cartridge.

Component	Function/composition
1 Sampling device a. Closed position b. Lifted position	For collection of patient sample or control.
2 Capillary	1.5 µL capillary to be filled with sample material.
3 Reaction container a. Conjugate b. Membrane tube c. Washing solution d. Reconstitution reagent e. Empty	Contains reagents necessary for one test: Patented blue boronic acid conjugate. Tube with a polyethersulfone membrane. Morpholine buffered sodium chloride solution with detergents and preservative. HEPES buffered sodium chloride with lysis and precipitation agents. N/A
4 Handle	For correct place to hold the Test Cartridge.
5 Barcode label	Contains assay and lot specific information for the Analyzer.
6 Optical reading area	Area for transmission measurement.
7 ID area	Space for written or labelled sample identification.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use.
- Do not use Test Cartridges after the expiry date or if the Test Cartridges have not been stored in accordance with recommendations.
- Do not use the Test Cartridge if the foil pouch or the Test Cartridge itself has been damaged.
- Each foil pouch contains a desiccant bag with 1 g silica gel. This material shall not be used in the assay. Discard the desiccant bag in a suitable container. Do not swallow.
- Do not use the Test Cartridge if the desiccant bag is damaged and desiccant particles are found on the Test Cartridge. Do not wipe off.
- Do not touch the Test Cartridge optical reading area (figure 1).
- In case of leakage, avoid contact with eyes and skin. Wash with plenty of water.
- Do not re-use any part of the Test Cartridge.
- The used Test Cartridges, sampling equipment, patient samples and controls are potentially infectious and should be disposed of immediately after use. Proper handling and disposal methods should be followed in accordance with local, state and federal regulations. Use personal protective equipment.

STORAGE AND STABILITY

Refrigerated storage 2-8°C (36-46°F)

- The Alere Afinion™ HbA1c Dx Test Cartridges are stable until the expiry date only when stored refrigerated in sealed foil pouches. The expiry date is the last day of the month stated on the foil pouch and outer container.
- The Alere Afinion™ HbA1c Dx Test Cartridge must reach an operating temperature of 18-30°C (64-86°F) before use. Upon removal from refrigerated storage, leave the Test Cartridge in the unopened foil pouch for at least 15 minutes. Information code 210 will be displayed and no test result obtained if the Test Cartridge is too cold when used.
- Do not freeze.

Room temperature storage 15-25°C (59-77ºF)

- The Alere Afinion™ HbA1c Dx Test Cartridges can be stored in unopened foil pouches at room temperature for 90 days. Note the date of removal from the refrigerator and the new expiry date on the kit container.
- Avoid exposure to direct sunlight.

Opened foil pouch

- The Test Cartridge should be used within 10 minutes after opening.
- Avoid exposure to direct sunlight.

SPECIMEN MATERIALS AND STORAGE

The following sample materials can be used with the Alere Afinion™ HbA1c Dx test:

- Capillary blood sample (from finger prick).
- Venous whole blood with anticoagulants: K2-EDTA, K3-EDTA, Li-Heparin, Na-Heparin, NaF/Na2-EDTA, NaF/K-oxalate, Na-citrate. EDTA=ethylene diamine tetra-acetic acid.

Specimen storage

- Capillary blood samples cannot be stored.
- Venous whole blood with anticoagulants (K2-EDTA, K3-EDTA, Li-heparin, Na-Heparin, Na-citrate) can be stored refrigerated (2-8°C) for 10 days or at room temperature (18-30°C) for 8 hours. Do not freeze.
- Consult the Alere Afinion™ HbA1c Control Package Insert for storage of control materials.

TEST PROCEDURE

The Alere Afinion™ HbA1c Dx Quick Guide provides detailed instructions on how to collect and analyze a patient sample or control.

Test procedure overview

- Switch on the Alere Afinion™ AS100 Analyzer.
- Allow the Alere Afinion™ HbA1c Dx Test Cartridge to reach operating temperature 18-30°C (64-86°F). Open the foil pouch just before use.
- Be sure to properly label the Test Cartridge with sample ID. The Test Cartridge has a dedicated ID area.
- Collect a specimen following the specimen collection procedure described below. Once the capillary is filled, analysis of the Test Cartridge must start within 1 minute.
- Insert the Test Cartridge in the Analyzer. The analysis time is approximately 3.5 minutes.
- Record the test results in the proper place according to the laboratory guidelines. The results will be stored in the Analyzer electronic result records.
- Remove the Test Cartridge from the Analyzer.

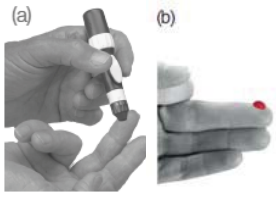
Important!

Do not use test cartridges that have been accidentally dropped on the floor or lab bench after specimen collection.

Specimen collection

Blood sampling from finger

- Always use gloves.
- Clean the finger using alcohol. Allow the area to air dry.
- Use a lancet and firmly prick the finger (a). Properly dispose the lancet.
- Allow a good drop of blood to form before sampling (b).



- Apply direct pressure to the wound site with a clean gauze pad.

Sampling from a tube

- Patient samples stored refrigerated can be used without equilibration to room temperature.
- Mix the sample material well by inverting the tube 8-10 times before collecting a sample.

Sampling from the Alere Afinion™ HbA1c Control vial

- Allow the control material to reach ambient operating temperature (18-30ºC, 64-86ºF) before use, which takes approximately 30 minutes.
- Mix the control material thoroughly by shaking the vial for 30 seconds. A whirl mixer may be used.
- Extract a sample from the vial or the cap.

Important!

- Bring the tip of the capillary just beneath the surface of the blood drop/sample material as shown in figures (a), (b) and (c).
- Be sure that the capillary is completely filled as shown in figure (d). It is not possible to overfill the capillary. Avoid air bubbles.
- Do not wipe off the capillary.

TEST RESULT REPORTING

Alere Afinion™ HbA1c Dx measures the total glycated hemoglobin and the total hemoglobin concentration. The ratio between them is proportional to the % HbA1c of the sample. The Analyzer calculates the ratio, and the test result is displayed as % HbA1c.

The Alere Afinion™ HbA1c Dx reportable range is 4.00-15.00% HbA1c. The HbA1c results are displayed in 0.01% intervals. The hemoglobin measuring range is 6-20 g/dL.

If the patient's HbA1c or hemoglobin value is outside range, no test result will be reported and the corresponding information code will be displayed. If accurate results outside the Alere Afinion™ HbA1c Dx range are required, the sample must be analyzed using another method.

Expected values

The diagnostic cut-off is 6.5 % HbA1c. Patients with HbA1c values in the range 5.7-6.4 % are identified as having an increased risk for developing diabetes[2,9].

Interpretation of results

Despite a reliable internal process control of the analysis, each individual test result should be interpreted with careful consideration to the patient's medical history, clinical examinations and other laboratory results. If the test result is questionable or if clinical signs and symptoms appear inconsistent with the test result, analyze the Alere Afinion™ HbA1c Controls and re-test the specimen.

Analytical specificity

Alere Afinion™ HbA1c measures the total glycated hemoglobin and reports the HbA1c value. No significant interference (< 7%) was observed for samples with hemoglobin (Hb) variants and hemoglobin derivatives up to the following concentrations:

- HbA2 5%
- HbAC 32%
- HbAD 40%

• HbAE	24%
• HbAS	39%
• HbF	7%
• Acetylated Hb	4.6 mg/mL
• Carbamylated Hb	13.8 mg/mL
• Labile (pre-glycated) Hb	11.4 mg/mL

Limitations of the test

This test should not be used to diagnose:
- diabetes during pregnancy
- patients with an elevated fetal hemoglobin (HbF >7%) such as hereditary persistence of fetal hemoglobin (HPFH)
- patients with a hemoglobinopathy but normal red cell turnover (e.g. sickle cell trait)
- patients with abnormal red cell turnover (e.g., anemias from hemolysis and iron deficiency)
- patients with iron deficiency and hemolytic anemia, various hemoglobinopathies, thalassemias, hereditary spherocytosis, malignancies, and severe chronic hepatic and renal disease
- patients that have received a blood transfusion within the past 3 weeks
- patients that have received cancer chemotherapy within the past 3 weeks

In cases of rapidly evolving type 1 diabetes the increase of HbA1c values might be delayed compared to the acute increase in glucose concentrations. In these conditions diabetes mellitus must be diagnosed based on plasma glucose concentration and/or the typical clinical symptoms.

HbA1c testing should not replace glucose testing for type 1diabetes, in pediatric patients and in pregnant women.

- Diluted samples cannot be used with Alere Afinion™ HbA1c Dx.
- Coagulated or hemolyzed samples cannot be used with Alere Afinion™ HbA1c Dx.
- If the sample has a hemoglobin value below 6 g/dL or above 20 g/dL, no test result will be reported and an information code will be displayed.

Interference

No significant interference (< 7%) was observed up to the following concentrations:

• Bilirubin conjugated	600 mg/L
• Bilirubin unconjugated	600 mg/L
• Glucose	10 g/L
• Lipids (as Intralipid)	10 g/L
• Rheumatoid factor	780 000 IU/L
• Total protein	150 g/L
• Glycated albumin	7.7 g/L

Over-the-counter and prescription drugs:

• Acetaminophen	200 mg/L
• Acetylcysteine	1663 mg/L
• Acetylsalicylic acid	1000 mg/L
• Ampicillin	1000 mg/L
• Ascorbic acid	300 mg/L
• Cefoxitin	2500 mg/L
• Cyclosporine A	5 mg/L
• Cyclosporine C	5 mg/L
• Doxycycline	50 mg/L
• Glyburide	1.9 mg/L
• Heparin	5000 U/L
• Ibuprofen	500 mg/L
• Levodopa	20 mg/L
• Metformin	40 mg/L
• Methyldopa	20 mg/L

• Metronidazole	200 mg/L
• Phenylbutazone	400 mg/L
• Rifampicin	64 mg/L
• Salicylic acid	599 mg/L
• Theophylline	100 mg/L

- Hemolysis (*in vitro*) 14%
- Anticoagulants (K2-EDTA, K3-EDTA, Li-Heparin, Na-Heparin, NaF/Na_2-EDTA, NaF/K-oxalate and Na-citrate) at concentrations normally used in blood collection tubes do not interfere.

Important!
It is possible that other substances and/or factors not listed above may interfere with the test and cause false results.

QUALITY CONTROL

Quality control testing should be done to confirm that your Alere Afinion™ AS100 Analyzer System is working properly and providing reliable results. Only when controls are used routinely and the values are within acceptable ranges can accurate results be assured for patient samples.

Each laboratory site can benefit from establishing a quality control plan. The laboratory director should determine whether additional testing is appropriate for their laboratory.

It is recommended to keep a permanent record of all quality control results. The Alere Afinion™ AS100 Analyzer automatically stores the control results in a separate record. Consult the Alere Afinion™ AS100 Analyzer User Manual.

Control material

Alere Afinion™ HbA1c Control from Alere is recommended for routine quality control testing. Consult the Alere Afinion™ HbA1c Control Package Insert.

Frequency of control testing

Controls should be analyzed:

- With each new shipment of Alere Afinion™ HbA1c Dx test kits.
- With each new lot of Alere Afinion™ HbA1c Dx test kits.
- At least every 30 days.
- When training new operators in correct use of the Alere Afinion™ HbA1c Dx and the Alere Afinion™ AS100 Analyzer.
- Anytime an unexpected test result is obtained.

If local, state and/or federal regulations require more frequent testing of control materials, then quality control should be performed in compliance with these regulations.

Verifying the control results

The measured value should be within the acceptable limits stated for the control material. Consult the Alere Afinion™ HbA1c Control package insert.

If the result obtained for the Alere Afinion™ HbA1c Control is outside the acceptable limits, make sure that:

- patient samples are not analyzed until control results are within acceptable limits.
- the control vial has not passed its expiry date.
- the control vial has not been in use for more than 60 days.
- the control vial and Alere Afinion™ HbA1c Dx Test Cartridges have been stored according to recommendations.
- there is no evidence of bacterial or fungal contamination of the control vial.

Correct any procedural error and re-test the control material.
If no procedural errors are detected:

- Examine the laboratory's quality control record to investigate the frequency of control failures.
- Ensure that there is no trend in out-of-range quality control results.
- Re-test the control material using a new control vial.
- Patient results must be declared invalid when controls do not perform as expected. Contact your customer service representative for advice before analyzing patient samples.

TROUBLESHOOTING

To ensure that correct HbA1c results are reported, the Alere Afinion™ AS100 Analyzer performs optical, electronic and mechanical controls of the capillary, the Test Cartridge and all individual processing steps during the course of each analysis. When problems are detected by the built-in failsafe mechanisms, the Analyzer terminates the test and displays an information code.

The table below contains Alere Afinion™ HbA1c Dx specific information codes. Consult the Alere Afinion™ AS100 Analyzer User Manual for information codes not listed in this table.

Code #	Cause
103	The hemoglobin concentration is below 6.0 g/dL
104	The hemoglobin concentration is above 20.0 g/dL
105	The HbA1c value is below 4.00%
106	The HbA1c value is above 15.00%

Follow the actions listed in the User Manual to correct the error.

Important!
The manufacturer must be notified of any test system that is perceived or validated to be outside of the performance specifications outlined in the instructions.

Technical support

The manufacturer provides a toll free line for technical support.
Call 1-866-216-9505. The toll free number is available for use only in the United States of America. E-mail: afinion.support@alere.com

PERFORMANCE CHARACTERISTICS

Linearity

The linearity of the Alere Afinion™ HbA1c Dx assay was verified using two fresh EDTA blood samples. Varying amounts of sample 1 (17.9% HbA1c) and sample 9 (5.3% HbA1c) were mixed in different proportions to obtain a total of 9 samples. Sample 2-8 were analyzed in triplicate, while sample 1 and sample 9 (native samples) were analyzed in six replicates. A linear regression was calculated based on the theoretical vs. measured % HbA1c values. The results are shown in Table 1.

Table 1: Linear regression of Alere Afinion™ HbA1c Dx: measured vs. theoretical (x) % HbA1c values. N=number of samples, r=correlation coefficient.

N	Regression line	r
9	y=1.01x + 0.07	1.00

The mean recovery of the measured % HbA1c values compared to the theoretical values (Table 2), were calculated for each sample, using the following equation:

$$\text{Mean recovery, (\%)} = \frac{\text{Measured mean value (\% HbA1c)} \times 100\%}{\text{Theoretical value (\% HbA1c)}}$$

Table 2: Linearity of Alere Afinion™ HbA1c Dx. Theoretical and measured mean value (% HbA1c), Coefficient of Variation (CV) and recovery mean value.

Sample	Theoretical (% HbA1c)	Measured (% HbA1c)	CV (%)	Recovery (%)
1*	N/A	17.9	3.8	N/A
2	14.1	14.2	2.0	101
3	12.9	13.3	0.4	103
4	11.6	11.8	2.5	102
5	10.3	10.4	1.5	101
6	9.1	9.2	2.3	101
7	7.8	8.0	1.3	102
8	6.6	6.6	2.6	101
9*	N/A	5.3	2.1	N/A

*Native sample
N/A Not applicable

Method comparison

Fingerstick and venous whole blood samples from 120 patients (4.6-11.4% HbA1c), 38-42 at each of three sites, were analyzed using three different Alere Afinion™ HbA1c Dx lots. The venous samples were sent to a laboratory for duplicate analysis with an HPLC method. The results are shown in Table 3 and Table 4.

Table 3: Method comparison. Alere Afinion™ HbA1c Dx vs. a laboratory HPLC method. Weighted Deming regression slope and intercept for 120 fingerstick samples (3 sites, 3 lots).

	Estimate	95% lower bound	95% upper bound
Slope	1.00	0.97	1.03
Intercept (% HbA1c)	0.00	-0.22-0.21	0.20

Table 4: Method comparison. Alere Afinion™ HbA1c Dx vs. a laboratory HPLC method. Weighted Deming regression slope and intercept for 120 venous whole blood samples (3 sites, 3 lots).

	Estimate	95% lower bound	95% upper bound
Slope	0.99	0.96	1.02
Intercept (% HbA1c)	0.05	-0.16	0.27

Precision

Internal study performed at Alere Technologies AS

Within device (total) precision was determined according to CLSI Protocol EP05-A2. Alere Afinion™ HbA1c Control C I, Control C II, and four EDTA whole blood samples were analyzed for 10 days, 2 runs per day and 4 replicates per run. 3 lots of Alere Afinion™ HbA1c Dx were used. Precision data are summarized in Table 5.

Table 5: Within device (total) precision Alere Afinion™ HbA1c Dx. N=number of replicates per lot=80. CV=Coefficient of Variation.

Sample	Lot 1		Lot 2		Lot 3	
	% HbA1c	CV (%)	% HbA1c	CV (%)	% HbA1c	CV (%)
Low	5.16	0.9	5.08	0.9	5.03	1.1
Threshold	6.47	1.1	6.38	1.0	6.37	0.9
Medium	8.42	1.0	8.37	1.1	8.37	0.9
High	11.82	1.0	11.81	0.9	11.78	1.2

External study

The precision of the Alere Afinion™ HbA1c Dx was assessed at three study sites. Each site tested four levels of HbA1c in venous whole blood specimens (one sample at each level): low, medium, threshold and high. Three lots of Alere Afinion HbA1c Dx were evaluated at each of the three study sites. Each specimen was analyzed in quadruplicate on each of the three Alere Afinion HbA1c Dx lots, two times per day for 10 consecutive days, resulting in 240 determinations per specimen. Within run (repeatability), between run, between day and total % CV was calculated. The results are shown in Table 6.

In addition, each site also tested two levels of controls in the same manner as the venous whole blood specimens. The control sample results are shown in Table 12.

Table 6: Root-mean-squared coefficient of variation (CV) across the three study sites and three lots of Alere Afinion HbA1c Dx.

Sample	% HbA1c range	%CV Within run	%CV Between run	%CV Between day	%CV Total
Low	4.74-5.24	1.2	0.2	0.1	1.5
Threshold	6.18-6.62	1.1	0.1	0.1	1.3
Medium	7.90-8.48	1.1	0.0	0.0	1.2
High	11.81-12.36	1.0	0.1	0.0	1.0

Between instruments precision

Between instruments precision of the Alere Afinion™ HbA1c Dx was evaluated for 4 whole blood samples on 14 Alere Afinion™ AS100 Analyzers. For each sample, 6 replicates were analyzed on each analyzer with one test cartridge lot. The results are shown in Table 7.

Table 7: Alere Afinion™ AS100 Analyzer between instrument precision. Mean % HbA1c and coefficient of variation (CV) of six replicates.

Sample	% HbA1c	Between instruments CV (%)
Low	5.46	0.7
Low	5.47	0.9
Threshold	6.54	0.8
Medium	8.85	1.0

Lot-to-lot variation

Lot-to-lot variation was evaluated with 18 whole blood samples and 3 lots of Alere Afinion™ HbA1c Dx. Each sample was tested in one replicate with each of 3 lots of Alere Afinion™ HbA1c Dx, using one Afinion™ AS100 Analyzer for all three lots. The results are shown in Table 8.

Table 8: Bias and 95% limits of agreement calculated for three lots of Alere Afinion™ HbA1c Dx using the Bland-Altman analysis

Lot no vs. lot no	N	Relative bias (%)	95 % limit of agreement
3-1	18	0.08	-3.5 to 3.7
2-1	18	-0.17	-4.0 to 3.6
3-1	18	0.25	-4.4 to 4.9

Total error

Total error (TE) was calculated using the %bias estimates in the external method comparison study and the precision estimates in the external precision study. %TE is computed according to the following formula:

$$\%TE = |\%Bias| + 1.96 \times \%CV \times \left(1 + \frac{\%Bias}{100}\right)$$

Total error was calculated for both fingerstick and venous samples at four %HbA1c levels. The results are shown in Table 9 and Table 10.

Table 9: %Total error (%TE) for fingerstick specimens.

Sample	% HbA1c Nominal value	%Bias	CV (%)*	%TE
Low	5.0	-0.34	1.45	3.16
Threshold	6.5	-0.33	1.27	2.81
Medium	8.0	-0.33	1.16	2.60
High	12.0	-0.33	0.98	2.25

*:CV (coefficient of variation) are estimates for venous whole blood.

Table 10: %Total error (%TE) for venous whole blood specimens.

Sample	% HbA1c Nominal value	%Bias	CV (%)	%TE
Low	5.0	0.20	1.45	3.04
Threshold	6.5	-0.05	1.27	2.53
Medium	8.0	-0.21	1.16	2.48
High	12.0	-0.43	0.98	2.35

Precision Alere Afinion™ HbA1c Control

Internal study performed at Alere Technologies AS

Within device (total) precision was determined according to CLSI Protocol EP05-A2. Alere Afinion™ HbA1c Control C I and Control C II were analyzed for 10 days, 2 runs per day and 4 replicates per run. 3 lots of Alere Afinion™ HbA1c Dx were used. Precision data are summarized in Table 11.

Table 11: Within device (total) precision Alere Afinion™ HbA1c Dx. N=number of replicates per lot=80. CV=Coefficient of Variation.

Sample	Lot 1		Lot 2		Lot 3	
	% HbA1c	CV (%)	% HbA1c	CV (%)	% HbA1c	CV (%)
Control C I	6.34	0.8	6.11	0.9	6.15	0.8
Control C II	8.34	0.9	8.49	0.7	8.35	0.7

External study

The precision of the Alere Afinion™ HbA1c Control was assessed at three study sites. Each site tested the two levels of controls: Control CI and Control CII. Three lots of Alere Afinion HbA1c Dx were used at each of the three study sites. The controls were analyzed in quadruplicate on each of the three Alere Afinion HbA1c Dx lots, two times per day for 10 consecutive days. Within run, between run, between day and total % CV was calculated. The results are shown in Table 12.

Table 12: Root-mean-squared coefficient of variation (CV) across the three study sites and three lots of Alere Afinion HbA1c Dx. N=number of determinations.

Sample	N	%CV Within run	%CV Between run	%CV Between day	%CV Total
Control C I	718	0.9	0.0	0.2	0.9
Control C II	720	0.8	0.0	0.1	0.8

SYMBOLS

The following symbols are used in the packaging material for Alere Afinion™ HbA1c Dx.

CE	Conformity to the European directive 98/79/EC on *in vitro* diagnostic medical devices
IVD	*In vitro* Diagnostic Medical Device
REF	Catalog number
LOT	Lot number
TEST CARTRIDGE	Test Cartridge
	Contents are sufficient for one test
	Contents sufficient for 15 tests
	Consult instructions for use
	Warnings and precautions
	Expiration date (year-month)
2°C 36°F 8°C 46°F	Storage temperature (store at 2-8°C, 36-46°F)
	Manufacturer
Int.	Internal lot number
Rx only	Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

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XXXXXX Rev. A 20XX/XX

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Alere Afinion™ HbA1c Dx Quick Guide

CLIA statement

Alere Afinion™ HbA1c Dx is categorized as a moderately complex assay under the Clinical Laboratory Improvement Amendment of 1988 (CLIA`88).

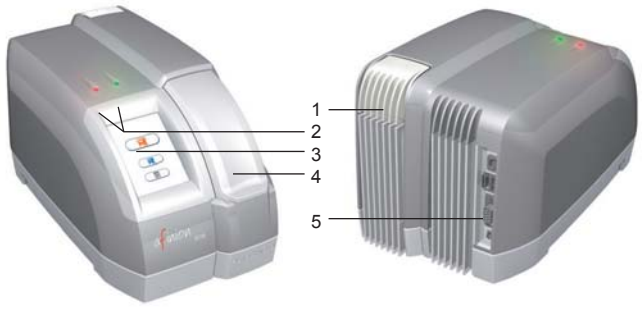
Important!

- Read the entire Alere Afinion™ HbA1c Dx Quick Guide before testing patient samples or controls.
- See the Alere Afinion™ AS100 Analyzer User Manual for more information about the operation of the Analyzer and Test Cartridge.
- See the Alere Afinion™ HbA1c Dx Package Insert for more information about the HbA1c assay.
- Use quality control materials to confirm that the Analyzer and test kit are working properly.

1 Getting Started

Read the entire Alere Afinion™ HbA1c Control Package Insert before use.

Alere Afinion™ AS100 Analyzer



1 ON/OFF button
2 Light emitting diodes
3 Touch screen
4 The lid
5 Connectors

Cleaning the Analyzer

Clean the Analyzer every 30 days. Follow the procedure in the User Manual. See section “Cleaning and Maintenance”.

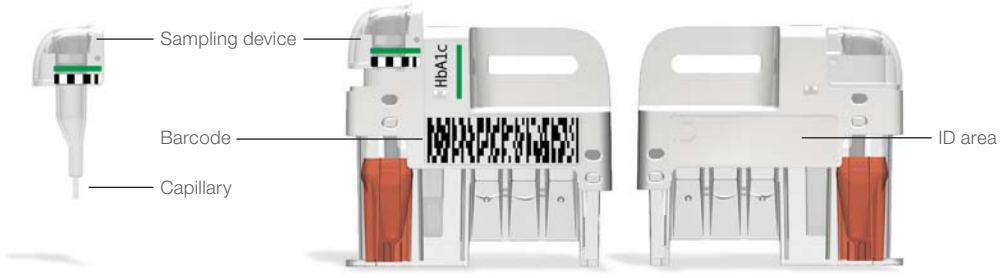
Important Touch Buttons

- Patient sample mode
- Control mode
- Patient ID
- Control ID
- Enter
- Accept

Product Specific Information Codes

Code	Cause
103	Hemoglobin below 6.0 g/dL
104	Hemoglobin above 20.0 g/dL
105	HbA1c below 4.00%
106	HbA1c above 15.00%

Alere Afinion™ HbA1c Dx Test Cartridge



2 Prepare for Testing

- Switch the Analyzer on.
- Allow 15 minutes for the Test Cartridge to reach operating temperature (64-86°F) before use.
- Open the pouch just before use. Hold the Test Cartridge by the handle.
- Label the Test Cartridge with sample ID. Use the ID area.
- Analyze **Alere** Afinion™ HbA1c Control before analyzing patient samples.

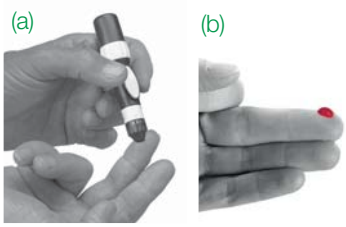
3 Procedure for Collecting the Sample

Sampling from a Control Vial

Follow the procedure described below. See page 4 for control testing recommendations.

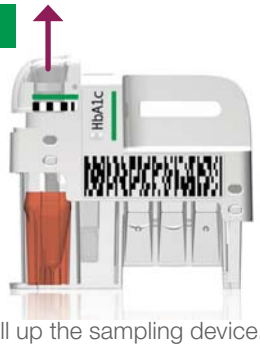
Sampling from Finger

- Always use gloves.
- Cleanse the finger using alcohol. Allow the area to air dry.
- Use a lancet and firmly prick the finger (a). Properly dispose the lancet.
- Allow a good drop of blood to form before sampling (b).
- Apply direct pressure to the wound site with a clean gauze pad.



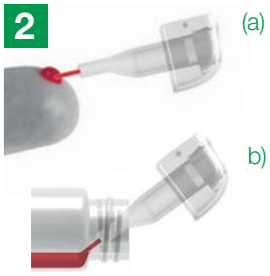
Specimen Collection using the Alere Afinion™ HbA1c Dx Test Cartridge

1



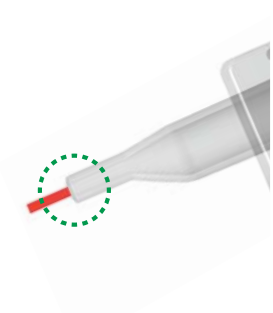
Pull up the sampling device.

2



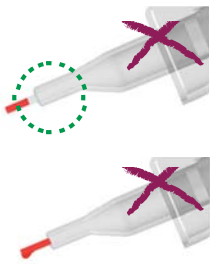
Touch the surface of the blood drop (a) or control (b).

3



Fill the capillary to the end. It is not possible to overfill.

4



Avoid air bubbles and incomplete filling (a). Avoid sample on the outside of the capillary (b). Do not wipe off.

5

Insert the sampling device immediately.

6

Within 1 minute place the Test Cartridge in the Analyzer.

4 Running Samples on the Analyzer

Patient Sample:
Touch  for patient samples.

Control:
Touch  for controls.

The lid opens automatically.
Insert the Test Cartridge.
The barcode should face left.

Close the lid manually.

Patient Sample:
Touch  for patient samples.

Control:
Touch  for controls.

Enter ID during processing.

Touch  to confirm.

Record the result when it appears on the screen.

Touch  to accept.

The lid opens automatically.
Remove and discard the Cartridge.

Close the lid manually.

Information Codes

Important information codes are listed on page 1. Consult the Analyzer User Manual for information codes not listed on page 1. Follow the actions listed in the User Manual to correct the error.

Verification of Test Results

Consult the Alere Afinion™ HbA1c Dx Package Insert. See section “Test result reporting”.

Verification of Control Results

Compare the results with the values listed on the front of the Alere Afinion™ HbA1c Control Package Insert.

Technical Support?

Call 1-866-216-9505. This is a toll free number.
Available for use only in the United States of America.

Control Testing

Read the entire Alere Afinion™ HbA1c Control Package Insert before use.

How often do I have to run controls?

It is recommended analyzing controls:

- With each new shipment of HbA1c Dx kits.
- With each new lot of HbA1c Dx kits.
- At least every 30 days.
- When training new users.
- Anytime an unexpected test result is obtained.

How should I use the Alere Afinion™ HbA1c controls?

- Allow the control to reach room temperature before use. This takes about 30 minutes.
- Mix the control well by thoroughly shaking the vial for 30 seconds. A whirl mixer may be used.
- Inspect the vial to ensure that the control solution is homogenous.
- Analyze the control using the procedures described on page 2 (Specimen Collection) and page 3 (Running Samples on the Analyzer).
- Compare the test results with the values listed on the front page of the Alere Afinion™ HbA1c Control Package Insert.

What do I do if Alere Afinion™ HbA1c Control results are not within the acceptable range?

- Do not analyze any patient samples.
- Check the control vial label to make sure it is not expired.
- Ensure that the control has not been used for more than 60 days.
- Verify that the controls and test cartridges have been stored correctly.
- Verify that there is no visual sign of bacterial or fungal growth in the control vial.

Correct any procedural error. Re-test the control.

If the control values are still not within acceptable range, repeat the test using a new vial of control. If the control results are still not acceptable, call Technical Support.

Technical Support?

Call 1-866-216-9505. This is a toll free number.
Available for use only in the United States of America.

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Rev: xxxxxxxxxxxxx

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Alere Afinion™
AS100 Analyzer

US

CE

REF 1115175/1115390, 111XXXX

111XXXX Rev. A 2015/11 DRAFT 1

Dear Customer,

Congratulations on the purchase of your Alere Afinion™ AS100 Analyzer.

Upon arrival of your Alere Afinion™ AS100 Analyzer we recommend that the serial number along with the software version be recorded in the table provided below. The additional rows in the table are to be utilized if a software upgrade is performed on your AS100 Analyzer. The recorded information will be of great value if and when a question is reported, or the desire to add a new Alere Afinion™ test to your Analyzer arises.

Serial number

SN _____ (see label on the underside of the Analyzer or on the transport container)
NOTE! The Analyzer must be turned off when the label on the underside is read.

Software records

	Date	Software version*	Alere Afinion™ tests available
Upon receipt			
1. SW upgrade			
2. SW upgrade			
3. SW upgrade			
4. SW upgrade			
5. SW upgrade			

* See start-up menu when you power on the Analyzer (see “How to power on the Analyzer”, page 10).

Notes

Technical Support

Call 1.866.216.9505

Alere Afinion™ AS100 Analyzer System

Intended use

Alere Afinion™ AS100 Analyzer with Alere Afinion™ Data Connectivity Converter (ADCC) is a compact multi-assay analyzer for point-of-care testing, designed to analyze the Alere Afinion™ Test Cartridges. The ADCC is a small device for automatic transfer of data, including patient and control assay results, from the Alere Afinion™ Analyzer to a laboratory information system or another electronic journal system. Alere Afinion™ AS100 Analyzer System, consisting of Alere Afinion™ AS100 Analyzer with Alere Afinion™ Data Connectivity Converter (ADCC), Alere Afinion™ Test Cartridges and Alere Afinion™ Controls is for in vitro diagnostic use only.

CLIA Statements

CLIA waived Alere Afinion™ AS100 Analyzer system

Analyzers configured for use with CLIA waived tests only:
REF 1115175/1115390 Alere Afinion™ AS100 Analyzer – CLIA waived version

Alere Afinion™ HbA1c is waived under the Clinical Laboratory Improvement Amendment of 1988 (CLIA`88).

A CLIA Certificate of Waiver is needed to perform testing in a waived setting.

If the laboratory does not have a Certificate of Waiver, the Application for Certification (Form CMS-116), can be obtained at https://www.cms.gov/cmsforms/downloads/cms116.pdf.
The form should be mailed to the address of the local State Agency of the State in which the laboratory resides (https://www.cms.gov/CLIA/12_State_Agency_&_Regional_Office_CLIA_Contacts.asp).

If the laboratory modifies the Alere Afinion™ test or Alere Afinion™ AS100 Analyzer system instructions, the test no longer meets the requirements for waived categorization.
A modified test is considered to be highly complex and is subject to all applicable CLIA requirements.

Moderately complex Alere Afinion™ AS100 Analyzer system

Analyzers configured for use with moderately complex tests and CLIA waived tests:
REF 111XXXX Alere Afinion™ AS100 Analyzer – Moderately complex version

Alere Afinion™ tests of moderate complexity should not be run in CLIA waived laboratories.

Conformity to the European IVD directive

The Alere Afinion™ AS100 Analyzer meets all provisions in the European directive 98/79/EC on In Vitro Diagnostic Medical Devices and is CE marked accordingly.

Safety standards

Alere Afinion™ AS100 Analyzer has been tested and found to be in conformity with IEC, UL, CAN/CSA-C22.2: 61010-1 (Safety requirements for electrical equipment for measurement, control, and laboratory use), IEC 61010-2-081:2001 + A1 and IEC 61010-2-101:2002 (Particular requirements for in vitro diagnostic (IVD) medical equipment).

EMC standards

Alere Afinion™ AS100 Analyzer has been tested and found to be in conformity with EN 61326-1:2006 (Electrical equipment for measurement, control, and laboratory use – EMC requirements) and EN 61326-2-6:2006 (In vitro diagnostic (IVD) medical equipment) and CFR 47 Telecommunications, Chapter I- FCC Part 15 – Radio Frequency Devices – Subpart B: unintentional radiators.

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ISO 13485 certified company

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About this User Manual

This User Manual will guide you through installation, operation and maintenance of your Alere Afinion™ AS100 Analyzer. The User Manual also explains how the Analyzer works, describes the quality assurance system and assists you in troubleshooting.

For analyzing patient samples or controls, please also read the test specific information given in the Package Inserts found in the Alere Afinion™ test kits. The Quick Guides highlight the main steps of the test procedures and contains information on proper quality control routines.

It is recommended that you become familiar with the user instructions before you start operating the Alere Afinion™ AS100 Analyzer.

Some of the information in this User Manual is accompanied with a symbol that points you to the following particulars:


Operator's handling


Warnings and precautions


References to the Package Inserts and Quick Guides for the specific Alere Afinion™ tests and control kits

Examining the package contents

When unpacking, check the contents against the list below and examine the components for signs of shipping damage.

The Alere Afinion™ AS100 package unit includes:

- Alere Afinion™ AS100 Analyzer
- Power cable
- Power cord adapter, 24 volt power supply
- Quick Guides for the available Alere Afinion™ tests
- User Manual
- Installation video (CD-ROM)

If the package unit is found incomplete, please report missing items or shipping damage to your supplier. It is recommended to keep the shipping box in case of later transportation of the Analyzer.

Description of the Alere Afinion™ AS100 Analyzer

Figure 1 shows the main exterior parts of the Alere Afinion™ AS100 Analyzer.

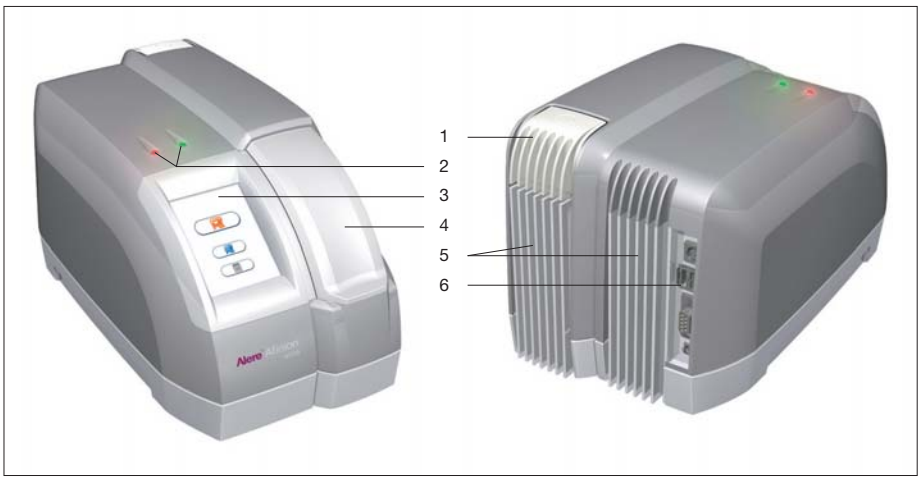


Figure 1

1	ON/OFF button:	Turns the power to the Analyzer on and off.
2	Red and green LEDs:	Light emitting diodes (LEDs) that indicate whether the Analyzer is busy or not.
3	Touch screen:	Allows you to communicate with the Analyzer through touch icons and messages.
4	The lid:	Covers and protects the cartridge chamber.
5	Cooling ribs:	Facilitate temperature control.
6	Connectors:	Connection to power cord adapter USB port- Options for printer, barcode reader, export of patient and control record to USB flash and SW upgrade. RS232- Connectivity options to EMR and/or HIS/LIS systems through the Alere Afinion™ Data Connectivity Converter (ADCC).

⚠ Do not open the lid manually.

Description of the Alere Afinion™ Test Cartridge

The Alere Afinion™ Test Cartridge is unique for each analyte to be measured, as the reagent composition, reagent volumes and the integrated devices are test specific. The Test Cartridge and the sampling device labels have a unique color for each test. The Test Cartridges are separately packed in foil pouches to protect the chemicals and plastic devices from light, dirt and humidity. A single Test Cartridge contains all necessary reagents for one test and is ready to use. An integrated sampling device is used for collection of the patient sample or control. The Test Cartridge cannot be re-used.

Figure 2 illustrates an Alere Afinion™ Test Cartridge with its functional parts:

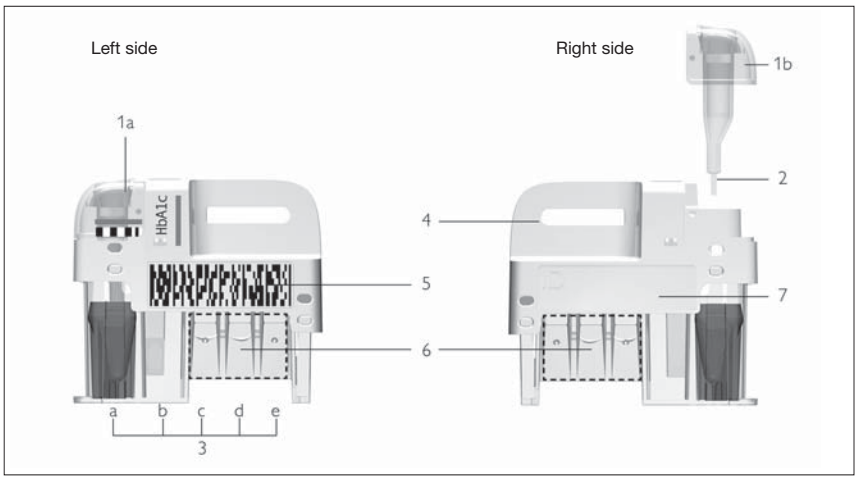


Figure 2

1	Sampling device:	For collection of patient sample or control. 1a - closed position 1b - lifted position
2	Capillary:	Capillary to be filled with sample material.
3	Reaction wells:	Contains all necessary reagents for one test.
4	Handle:	For correct finger grip.
5	Barcode label:	Contains assay and lot specific information for the Analyzer.
6	Optical reading area:	Area for transmission measurement.
7	ID area:	Space for written or labeled sample identification.

How the Alere Afinion™ AS100 Analyzer System works

The Alere Afinion™ AS100 Analyzer System uses different chemical and mechanical assay methods combined with advanced, computerized processing and measuring technology.

A Test Cartridge with patient sample or control is placed in the cartridge chamber of the Analyzer. By manually closing the lid, the Test Cartridge is transported into the analysis compartment of the Analyzer. Test and lot-specific information is obtained from the barcode label (Figure 2). When the Test Cartridge enters the Analyzer, the integrated camera reads the barcode. The calibration data for the actual lot are read, which then initiates the processing of the Test Cartridge. The sample and reagents are automatically transferred between the wells. An integrated camera monitors the entire process. Light-emitting diodes (LEDs) illuminate the reaction area, which can be either a colored membrane or a reaction well. The camera detects the reflected or transmitted light, which is converted to a test result and displayed on the touch screen. When the user accepts the result, the lid covering the cartridge chamber opens automatically and the used Test Cartridge can be removed and discarded. The Analyzer is then ready for the next run.

Internal process control

The Analyzer self-test

A self-test is performed during start-up of the Analyzer to ensure that the instrument is operating according to established specifications. The self-test validates:

- Hardware and software integrity
- Test Cartridge transport system
- Liquid transport system
- Camera vision system

If the self-test fails at any point the red LED will start flashing and an information code will be displayed on the touch screen (see “Information codes and troubleshooting”, page 27).

When the Analyzer is powered on for a longer period, it will automatically restart once a day to ensure that a self-test is done regularly. This procedure does not interrupt any analysis of the Test Cartridge.

The fail-safe mechanisms

Fail-safe mechanisms are included to secure safe processing. The integrated camera inspects the test cartridges initially before the process starts and during the assay. If defects are detected (e.g. broken capillary or the cartridge is used past its expiry date), the Test Cartridge is rejected and an information code is displayed. During processing vital functions and components (e.g. pumps and heater) are supervised. When problems are detected by the built-in safety mechanism, the process will be aborted and an information code will be displayed.

External process control

Patient ID

The Alere Afinion™ patient ID functionality will, if configured, allow up to four patient ID fields to be entered.
The Patient ID will be stored with each patient test result in the result records.

Operator ID

The Alere Afinion™ operator functionality will, if configured, require the operators to login before testing. The functionality may also prevent un-authorized operators to login, perform tests and configuration. The operator ID will be stored with each test result in the result records.

Quality Control lockout

The Alere Afinion™ QC lockout function allows you to configure the instrument to automatically enforce your local required frequency of control testing. If the required control test has not been performed or the control result is outside the acceptable range, the instrument will disable patient testing for this assay. For manufacturer recommendations (see “Frequency of control testing” page 18). For more information regarding these functionalities (see “Setting the configuration” page 13).

Calibration

The Alere Afinion™ AS100 Analyzer has been manufactured to deliver reliable and accurate results. During manufacturing, the Analyzers are calibrated against a reference system. This procedure has been established to ensure that all Analyzers operate within identical tolerance limits.

Test specific calibration data are established for each lot of Test Cartridges and then stored in the barcode label (Figure 2).
When the Test Cartridge enters the Analyzer, the integrated camera reads the barcode. The calibration data for the actual lot are transferred to the instrument and used for calculating the results. Calibration by the operator is thus not required.

Installing your Analyzer

Place your Alere Afinion™ AS100 Analyzer on a dry, clean, stable and horizontal surface. Make sure that the Analyzer is located with sufficient surrounding airspace, at least 5 inches on each side. Acclimate the Analyzer to ambient operating temperature (15-32°C, 59-89°F).

The Analyzer might be impaired by:

- Condensing humidity and water
- Heat and large temperature variations
- Direct sunlight
- Vibrations (e.g. from centrifuges and dishwashers)
- Electromagnetic radiation (e.g.from mobile phones)
- Movement of the Analyzer during processing of a Test Cartridge

Connecting power supply

- Connect the power cable to the power cord adapter.
- Insert the plug from the power cord adapter into the power socket (Figure 3) in the back of the Analyzer.
- Plug in the power cord to a wall outlet.

Always use the correct supply voltage. The power supply voltage must match the information quoted in the section “Technical specifications”, page 32.

Figure 3

1 Not in use
2 USB-A connectors for printer, USB flash and/or barcode reader
3 RS-232 port for connection to HIS or LIS systems.
4 Power input for power supply connection

Connecting additional equipment

Optional equipment, not provided with your Alere Afinion™ AS100 Analyzer are:

- External barcode reader – for reading barcoded sample or operator identification.
- Printer – for optional print out of test results.
- Alere Afinion™ Data Connectivity Converter - For data transfer to HIS or LIS systems (see “Additional equipment”, page 32).

For additional information regarding the barcode reader, printer, and connection to HIS or LIS systems, please contact your local Alere Afinion™ supplier.

Connecting the equipment should be done while the Analyzer is powered off.

How to power ON the Analyzer

1 

Power on the Analyzer by pressing the ON/OFF button (Figure1). An automatic start-up procedure will be initiated. Please wait.
Do not open the lid manually.

2 

The automatic start-up procedure will be initiated shortly after the Analyzer has been powered on. The red light on the top of the Analyzer will turn on, indicating that the Analyzer is busy.

If the Analyzer is configured for use with CLIA waived tests only, "CLIA WAIVED" will be displayed next to the SW version (SW X.XX CLIA WAIVED) in the upper left corner of the screen during the automatic start-up procedure.
If the Analyzer is of moderate complexity, the Analyzer will allow for the use of both moderately complex and CLIA waived tests.
The Analyzer is ready for use when the start-up menu is displayed and the green indicator light turns on.

3 

Start-up menu

The Analyzer's software version (SW X.XX) will appear in the upper left corner of the Start-up menu screen. The temperature displayed in the Start-up menu is the operating analyzer temperature. Make sure that the operating temperature is within the recommended range for your Alere Afinion™ test (see the Package Insert for the Alere Afinion™ test).
If the Analyzer fails during the start-up procedure, an information code will appear referring to a message given in the "Information codes and troubleshooting", page 27–29.

How to power OFF the Analyzer

Power off the Analyzer by pressing the ON/OFF button (Figure 1). The Analyzer should be powered off after the end of a working day.

Please note:

- When the power is turned off, a closing down procedure is initiated. The cartridge carriage will move to a safe position and the display will be active a few seconds while the Analyzer shuts down. The Analyzer can be powered off, or the power supply disconnected, without loss of stored results.
- The Analyzer can only be powered off when the cartridge chamber is empty and the lid is closed. If the ON/OFF button is pressed and the lid is open, the message "Close lid" will appear on the screen.

How to operate the Analyzer

The Alere Afinion™ AS100 Analyzer has two main user interfaces, the touch screen and the cartridge chamber. The Analyzer is easily operated using the touch buttons that appear on the screen. When a button is touched, its function will be activated. Text messages that appear on the screen will help guide you through the testing procedure. The functions of the touch buttons are explained in the “Gallery of icons”, page 33–35.

The other main operative part of the Alere Afinion™ AS100 Analyzer is the cartridge chamber. The cartridge chamber is designed to receive the Test Cartridge in one orientation only. The lid must be manually closed, but opens automatically. When a new Test Cartridge is placed in the chamber, manually closing the lid will initiate the analysis. When the analysis is complete the lid will open automatically. The lid protects the cartridge chamber from dust, dirt, light and humidity during processing and when the Analyzer is not in use.

⚠
- The lid must be manually closed, but opens automatically. Do not open the lid manually.
- Use the fingertips only on the touch screen. Do not use pens or other sharp instruments.

Figure 4

1 Text message
2 Touch buttons
3 The lid in open position
4 The cartridge chamber with a Test Cartridge

Screen saver

The screen saver will turn on after 3 minutes, if the touch screen is not in use. To re-activate, touch the screen.

Light signals (the red and green LEDs)

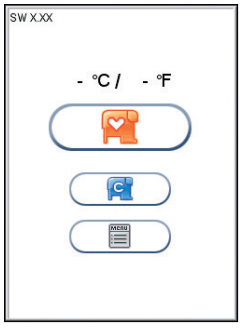
The red diode is illuminated when the Analyzer is busy. A flashing red light is seen when an information code is displayed.
The green diode is illuminated when the Analyzer is ready for use. A flashing green light indicates completion of an analysis.

Sound signals

A short beep indicates completion of an analysis. Two beeps mean that an information code or message is displayed.

The Alere Afinion™ Menus

Start-up menu

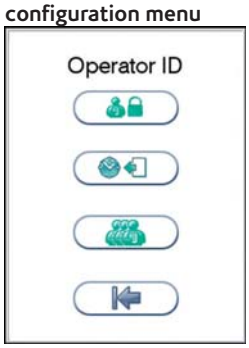


Main menu

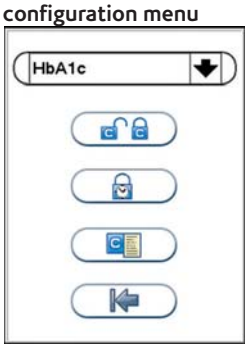
Configuration menu

Patient ID configuration menu

Operator configuration menu



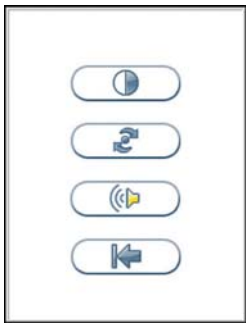
QC lockout configuration menu



Language settings

Date/Time Menu

Screen and beeper volume menu



Setting the configuration

Before using your Alere Afinion™ AS100 Analyzer you should set the configuration according to your needs. To enter the configuration menu, do the following:

1 

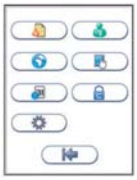
Start-up menu

Touch  to enter main menu.

2 

Main menu

Touch  to enter configuration menu.

3 

Configuration menu

Select an item for configuration (see following pages).

Patient ID configuration

Patient ID enable/disable

The patient identification (ID) function can be enabled or disabled. The patient ID function is enabled as a default setting by the manufacturer. When the patient ID function is enabled, the patient ID must be entered for each Test Cartridge to be analyzed. If the patient ID function is disabled, a run number will automatically replace the patient ID and be displayed in the upper left corner of the screen. This numbering is reset each day at midnight.

Touch  in the configuration menu to enter the patient ID on/off option.

Select ◉  to disable the patient ID function.

Select ◉  to enable the patient ID function.

Touch  to accept and return to the configuration menu.

Operator configuration

The Operator ID function is disabled as a default setting by the manufacturer.
Touch in the configuration menu to enter the operator configuration menu.

Operator ID enable/disable

Touch in operator configuration menu to enable/disable operator ID.

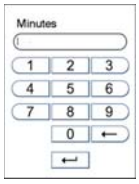
Select to disable the operator ID function.
Select to enable operator ID. Any operator ID is accepted.
Select to enable operator ID with verification.

- To enable this function at least one supervisor is required to be present in the operator list.
- When operator ID verified is enabled, instrument configuration will only be available to the supervisors.
- To log in, the operator ID entered is required to be present in the operator list (see “Operator management”, bottom of the page).

Touch to accept and return to the configuration menu.

Operator login expiration

Touch in the operator configuration menu to set automatic logout of the operator.



Enter the number of minutes before automatic logout of operator.
The operator will automatically be logged out after the configured number of minutes after analysis of the test is complete.
Touch to confirm and return to previous view.

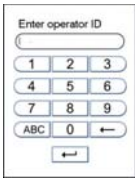
Operator management

Touch in operator configuration menu to enter operator list.

1

Touch to add new operator.
Touch desired operator ID and touch to delete or to edit the highlighted operator.

2



Enter new/edit operator ID

Enter new/edit operator ID and touch to enter. Both letters and numbers can be entered (maximum 16 characters).
If a barcode reader is connected to the Analyzer, a barcoded operator ID can be entered.

3

Configure the operator level:

Select whether this operator will be a user or supervisor.

1) User

2) Supervisor

Configure tests accessible by checking the appropriate test boxes for this operator.

Check off the test accessible for this operator.

Touch to return and edit the operator ID.

Touch to accept and store new operator in the operator list. The operator list can store 500 operator IDs.

*Supervisors will be marked with * in the operator list. When instrument is configured to Operator ID verified, configuration of instrument settings will only be available to the supervisors.*

Copy operator list

It is possible to copy operator lists between instruments using a USB flash drive. Insert USB flash in instrument USB port. Touch to export operator list from instrument to USB flash. Move USB to new instrument and touch to import operator list. Any existing operator list on the instrument will be deleted.

Choosing language

Touch in the configuration menu to enter the language selection. The default setting by manufacturer is English. Other languages are available.

Touch the arrow in the window to view other options. Scroll down until you find the preferred language.
Touch to accept and return to the configuration menu.

Setting date and time

The correct date and time should always be set because the date and time for the analyses are stored and displayed in the patient and control records. The date format is YYYY:MM:DD, where YYYY is the year, MM is the month (01 to 12), and DD is the day (01 to 31). The time format is hh:mm, where hh is the hour from 00 to 23 and mm is minutes from 00 to 59.

Touch in the configuration menu to enter date/time setting.

1

Touch to enter date setting.
Touch to enter time setting.

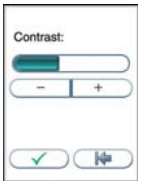
2

Enter today's date or time.
Touch to confirm and return to the previous view.

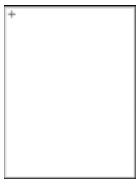
Adjusting screen/beeper volume settings

Touch in the configuration menu to enter the screen/beeper volume settings.
The screen contrast can be adjusted.

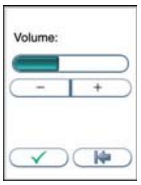
Touch to enter the screen contrast setting.
Touch to enter the screen alignment setting.
Touch to enter the beeper volume setting.



Screen contrast setting
Adjust the screen contrast by touching - or +
Touch to confirm and return to previous view.



Screen alignment setting
Tap the cross-hair object (+) in the upper left corner using a blunt pencil to be precise. Repeat for the object appearing in the lower right corner and in the center of the screen. The previous screen view will automatically return.



Beeper volume setting
Adjust the beeper volume by touching - or +
Touch to confirm and return to the previous view.

General settings menu

Touch in the configuration menu to enter the general settings menu.

Touch to erase all content and configurations.
All data will be permanently erased.

QC lockout configuration

The QC lockout function is disabled as a default setting by the manufacturer.
Touch in the configuration menu to enter the QC lockout setting menu.

Touch to configure QC lockout for the assay selected.
Touch to configure QC lockout interval.
Touch to view/add/delete stored control lots in the control lot database.

1

Select assay type

Touch the arrow in the window to open the drop down menu to select the assay type.

Touch the assay to select.

2

QC lockout

Select to disable the QC lockout function. No QC runs will be required for this assay

Select to enable the QC lockout function. It is required to run **ONE** passed control, control level C I **OR** C II, to reset the QC lockout interval.

Select to enable the QC lockout function. It is required to run **TWO** passed control, both control level C I **AND** C II, to reset the QC lockout interval.

Touch to confirm and return to the previous view.

3

QC lockout interval

Select RUN# to configure QC lockout interval by number of runs.

Select to configure QC lockout interval by hours.

Touch to enter/edit number of runs/hours to QC lockout.

[xx] displays the number of runs/hours configured in the QC lockout interval.

Touch to confirm and return to the previous view.

4

Control lot database

To add a control to the control lot database, the Alere Afinion™ Control Data is required.

The Alere Afinion™ Control Data is a numeric data string which contains all lot spesific data:

- Alere Afinion™ control lot number
- Control type (assay)
- Control level (C I or C II)
- Control expiry date
- Acceptable control range
- CRC (check sum to validate the previous data)

The Alere Afinion™ Control Data and its accompanying barcode is found in the Alere Afinion™ Control kit package insert. If the Alere Afinion™ Control Data is not available, contact your local supplier.

Touch and either manually enter the Control Data or if a barcode reader is connected to the Analyzer (recommended), scan the barcode. The Alere Afinion™ Control Data may also be entered before, during or after a control run. The control lot will automatically be stored in the database (see page 25).

Touch to delete selected lot number from the control lot database. When a control lot has reached its expiry date, the control will automatically be deleted from the instrument control database. The control lot database can store 100 control lots.

Why quality control testing?

Quality control testing should be done to confirm that your Alere Afinion™ AS100 Analyzer System is working properly and providing reliable results. Only when controls are used routinely and the values are within the acceptable ranges can accurate results for patient samples be assured.

Choosing control material

Controls recommended by manufacturer should be used for quality control of your the Alere Afinion™ AS100 Analyzer System. These control kits contain control materials with established acceptable ranges for the Alere Afinion™ AS100 Analyzer System.

Handling and testing controls

Consult the Package Insert that comes with each control kit for detailed instructions on handling and storage of the control material.

To run a control, follow the procedure in the section “Testing procedures”, page 19–26.

The measured value should be within the acceptable range stated on the control vial label or in the control package insert. If the control results are within the acceptable ranges, patient samples may be tested and results reported.

If the result obtained for a control is outside the acceptable limits, make sure that:
- The control vial has not passed its expiry date.
- The control vial has not passed its open vial expiry date.
- The control vial and Alere Afinion™ Test Cartridges have been stored according to recommendations.
- There is no evidence of bacterial or fungal contamination of the control vial.

Correct any procedural error and re-test the control material. If no procedural errors are detected, it is recommended to examine the laboratory’s quality control record to investigate the frequency of control failures. Ensure that there is no trend in out-of-range quality control results. Re-test the control material using a new control vial.

Patient results must be declared invalid when controls do not perform as expected. Contact your Technical service representative (1.866.216.9505) for advice before analyzing patient samples.

Frequency of control testing

Controls should be analyzed:
- When starting up an Alere Afinion™ AS100 Analyzer for the first time.
- With each new shipment of Alere Afinion™ test kits.
- With each new lot of Alere Afinion™ test kits.
- Users with a low frequency of testing should analyze controls at least every 30 days.
- When training new operators in correct use of the Alere Afinion™ AS100 Analyzer.
- Anytime an unexpected test result is obtained.
- After software upgrade of the Alere Afinion™ AS100 Analyzer.

The controls should always be analyzed if an unexpected test result is obtained (see the Alere Afinion™ test Package Insert, section Test result reporting). If local, state and/or federal regulations require more frequent testing of control materials, then quality control should be performed in compliance with these regulations. Each laboratory site can benefit from establishing a quality control plan. The laboratory director should determine whether additional testing is appropriate for their laboratory.

Operating precautions

When operating the Analyzer

- Use your fingertip to operate the touch screen. Do not use pens or other objects that may scratch or damage the screen. Exception: If the screen alignment function is required, you will need to use a blunt pencil.
- The lid opens automatically, but must be closed manually. Do not try to open the lid manually.
- The lid protects the cartridge chamber from dust, dirt, light and humidity. Empty the cartridge chamber and keep the lid closed when the Analyzer is not in use.
- If an information code appears on the screen during the analysis, please consult the “Information codes and trouble-shooting” section, page 27–29.
- Do not move the Analyzer when a Test Cartridge is being processed.

When handling the Test Cartridge

- Do not use Test Cartridges after the expiry date, or if the Test Cartridges are not stored in accordance with the recommendations.
- Do not touch the Test Cartridge optical reading area. Hold the Test Cartridge by the handle. (Figure 2).
- Do not use the Test Cartridge if the foil pouch, the desiccant bag or the Test Cartridge itself is damaged.
- The Test Cartridges must reach recommended operating temperature before use.
- Do not open the foil pouch until just before use. Once opened, the Test Cartridge has limited stability.
- Handle and dispose the Test Cartridges and sample collection equipment as potential biohazardous materials. Use gloves.
- Do not re-use any part of the Test Cartridge.

Consult the Package Insert that comes with each Alere Afinion™ test kit for assay specific information.

Preparing for an Alere Afinion™ analysis

- Allow the Alere Afinion™ Test Cartridges to reach the recommended operating temperature before use.
- Power on your Alere Afinion™ Analyzer so it is ready for the day’s first analysis.
- Enter the operator ID (optional). See procedure on page 22.
- The patient ID, control ID or Alere Afinion™ Control Data can be entered before or during processing of the Test Cartridge in the Analyzer. See procedures on page 21–25.

Consult the Package Insert that comes with each Alere Afinion™ test kit for assay specific information.

1

Open the foil pouch. Grip the handle and remove the Test Cartridge from the pouch.
Discard the desiccant bag and foil pouch in suitable waste containers.

When first opened, the Test Cartridge has limited stability.

2

Inspect the Cartridge. Do not use the Test Cartridge if it is damaged or if loose desiccant particles are found on the Test Cartridge.

Use the handle to avoid touching the optical reading area.

3

Mark the Test Cartridge with the patient or control ID. Use the ID area on the Test Cartridge. An ID label can also be used.

Do not write on the barcode label or allow it to become wet, dirty or scratched.
If an ID label is used, this must fit into the ID area.

If a barcode reader is connected to the Analyzer, a barcoded patient ID, control ID or Alere Afinion™ Control Data can be entered.

Collecting a sample

- The patient sample material and control material to be used are specific for each Alere Afinion™ test.
- The length of the capillary in the sampling device, and thereby the sample volume, might also vary for the different Alere Afinion™ tests.
- The time from filling the capillary until analysing the Test Cartridge must be as short as possible.
- Do not use the Test Cartridge if dropped on the bench or floor after the sample has been collected.

Consult the Package Insert that comes with each Alere Afinion™ test kit for assay specific information.

Examples:

1	2	3
		
Remove the sampling device from the Test Cartridge. *Use the handle to keep the Test Cartridge steady against the table and pull the sampling device straight up.*	Fill the capillary; hold the sampling device almost horizontally and bring the tip of the capillary in surface contact with the sample. Make sure that the capillary fills completely. It is not possible to overfill. Do not wipe off the capillary. *Avoid air bubbles and excess sample on the outside of the capillary.*	Immediately and carefully replace the sampling device into the Test Cartridge. *The time from filling the capillary until analysing the Test Cartridge must be as short as possible.*

Analyzing a patient/control sample

1

Touch to enter the patient sample mode.

Touch to enter the control mode. A “C” in the upper left corner indicates that the Analyzer is in the control mode.

The lid opens automatically.

If the lid is left open from the previous run and “Insert Cartridge” is displayed, this step is omitted and you can start with step 2.

2

Insert the Test Cartridge with the barcode label facing left.

Be sure that the Test Cartridge is correctly placed in the cartridge chamber.

3

Close the lid manually.The Analyzer will start processing the Test Cartridge.

The processing time depends on the test in use.

4

Touch and enter the patient ID.

Touch to confirm.

Touch and enter the control ID or Alere Afinion™ Control Data.

Touch to confirm.

Entering the patient ID, control ID or Alere Afinion™ Control Data will not interrupt the processing.

5

Record the result, then touch to accept.

If a printer is connected, touch to print the result.

The lid opens automatically.
The result will be saved in the result records.

6

Remove the used Test Cartridge from the cartridge chamber and discard it in a suitable waste container.

Insert a new Test Cartridge or close the lid manually.

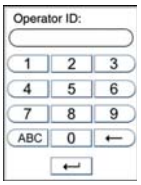
Keep the lid closed to protect the cartridge chamber when the Analyzer is not in use.

Consult the Package Insert that comes with each Alere Afinion™ test kit for assay specific information.

Using the operator ID function

Entering operator ID

If enabled, the operator's identification (ID) is required before processing an Alere Afinion™ Test Cartridge. (see "Operator Configuration" page 14).
Both letters and numbers can be entered (maximum 16 characters). The operator ID will be displayed with the result and stored along with the other specific data for this run (see "Patient and control results records", page 26).
If configured to "enabled with verification" the operator ID entered is required to be present in the operator ID list. (see "Operator configuration" page 14).



Enter the operator ID by numbers and/or touch ABC to enter letters. If a barcode reader is connected to the Analyzer, a barcoded operator ID can be entered.

Touch ↵ to confirm and return to previous view.

The operator will be automatically logged out according to the configuration. (see "Operator configuration" page 14).
The operator may also manually logout by using the operator logout button displayed in the Start-up menu.

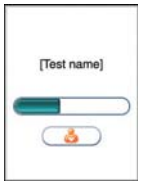
Using the patient ID function

The patient ID function is enabled as a default setting. As long as this function is enabled, the patient ID must be entered for each patient sample to be analyzed. The patient ID function can be disabled (see "Patient ID configuration", page 13).

Entering patient ID

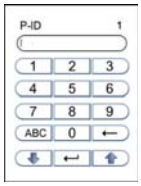
It is recommended to enter the patient ID during processing of the Test Cartridge in the Analyzer. Entering the patient ID will not interrupt the processing. It is also possible to enter the patient ID before and after the processing.

1



Touch to enter the patient ID option.

2



It is possible to enter up to four patient ID entries for each patient, P-ID 1 to 4. When enabled, P-ID 1 is required to be entered. Scrolling between the patient IDs is done with the and .

Enter patient ID by numbers and/or touch ABC to enter letters. (maximum 16 characters).
If a barcode reader is connected to the Analyzer, a barcoded patient ID can be entered.

Touch ↵ to confirm and return to previous view.

3

The entered P-ID 1 will appear on the screen.

The patient ID touch button will remain in the view and it is possible to make corrections.

The P-ID 1 will be stored in the memory and displayed along with the other specific data for this run (see "Patient ID configuration", page 13). Patient ID 2-4 will not be displayed in the result records but will be stored in the memory and appear on print outs and data transferred to data management systems.

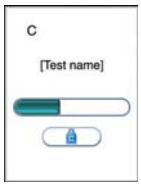
Using the control ID function

In quality control testing, a suitable control ID must always be entered. The lot number of the control material is recommended as a suitable control ID. The control ID function cannot be disabled.

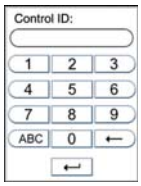
Entering Control ID

It is recommended to enter the control ID during processing of the Test Cartridge in the Analyzer. Entering the control ID will not interrupt the processing. It is also possible to enter the control ID before and after processing. Both letters and numbers can be entered (maximum 16 characters). The control ID will be displayed in the result records and appear on print outs and data transferred to data management systems.

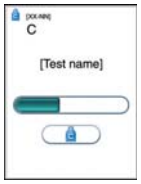
To enter the control ID during processing, do the following:

1 

Touch to enter the control ID option.

2 

Enter control ID by numbers and/or touch ABC to enter letters.
Touch to confirm and return to the previous view.

3 

The entered control ID will appear on the screen.
The control ID touch button will remain in the view and make corrections possible.

Using the QC lockout function

When the QC lockout function is enabled for one or more assays, approved control testing is required within the configured interval. If the interval expires, patient testing for the assay will be locked. A passed control run must be performed according to configuration, to reset the interval or to unlock the assay for patient testing. A failed control run will disable patient testing (see “Configuration of QC lockout” page 17).

QC lockout status

The status of the enabled QC lockouts is presented with a QC lockout status button (padlock symbol) visible in the Start-up menu. This gives the operator the status of QC lockout before he/she attempts to run any tests.
The padlock symbol will only be visible if QC lockout function is enabled for one or more assay types.

The padlock symbols used are:

1 

Enabled-unlocked

All controls are within the configured interval. It is possible to run patient tests for all assays.

2 

Warning-unlocked

All controls are within the configured interval. When one or more of the assays has 10 % or less of the configured interval remaining the warning icon will be displayed. It is possible to run patient tests for all assays.

3 

Expired-locked

One or more controls have expired according to the configured interval. Patient testing on the expired assay has been locked.

Touch the QC lockout status button (padlock symbol) in the **Start-up** menu to enter the QC lockout status view.

Status

The information is displayed as a list.

Only the assays with QC lockout activated are displayed in this window.

Red text indicates expired assays and orange text indicates assays within warning period.

Control level

How to reset QC lock interval and/or unlock expired assays.

4 

If no control level is specified, it is required to run **one** passed control, control level C I **or** C II, to reset the QC lockout interval and unlock the assay for patient testing.

E.g.

HbA1c: #0

If the control level is specified it is required to run **two** passed controls, both control level C I **and** C II, to reset the QC lockout interval and unlock the assay for patient testing.

E.g.

ACR C I: 00.00.00

ACR C II: 00.00.00

Remaining time/runs

Remaining time (dd:hh:mm) or number of runs for each assay with active QC lockout is shown. dd is the number of days, hh is the number of hours, and mm is the number of minutes until the assay will be locked. # is number of patient tests.

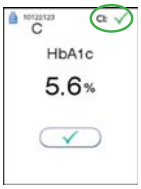
Running controls with enabled QC lockout function

When running controls with the QC lockout function enabled, the Alere Afinion™ Control Data is required to be entered or previously stored in the instrument control lot database (see “QC lockout configuration” page 17).

1) The Alere Afinion™ Control Data is entered before, during or after the control run. If a barcode scanner is connected (recommended) the Control Data barcode may be scanned. The control lot will automatically be stored in the instrument control database.

2) If the Alere Afinion™ Control Data is previously stored in the instrument control database, the operator will simply need to enter the 8 digit control lot number before, during or after the control run.

If the instrument is configured to QC lockout and the control lot number is not found in the Alere Afinion™ control database or the Alere Afinion™ Control Data entered is not valid, the instrument will present an option to retry the input or discard the control run result. If discarded, the result will not be stored in the instrument result records.

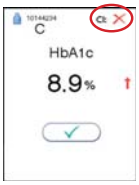


Passed (within the acceptable control range)

The result of the control is checked against the acceptable ranges for the corresponding lot number.

If the result is within the limits, a pass symbol ✓ is displayed on the screen and the QC lock interval is reset according to the QC lockout configuration. The result is stored in the instrument and is sent to the data management system if connected.

⚠ If QC lockout is configured to require two control levels (C I **and** C II), both levels must pass to reset the lockout interval. Only the interval for the control level used in the test is reset.



Failed (above or below the acceptable control range)

When a control result is not within the acceptable ranges specified for the control lot, a failed symbol ✗ is shown on the screen. The result is stored in the instrument and is sent to the data management system if connected. The QC lockout interval will not be reset.

The arrow symbol will specify whether the result is above ↑ or below ↓ the acceptable ranges (see “Handling and testing controls”, page 18).

Patient and control results records

The patient and control results are stored in the memory of the Alere Afinion™ AS100 Analyzer. The last 500 patient results and the last 500 control results are saved in separate records. When exceeding the capacity of 500 results, the oldest result will be deleted. The following parameters are listed for each run: Date and time, run number, patient ID/control ID, operator ID, lot number of Test Cartridge and the test result.

View, print and export patient and control results

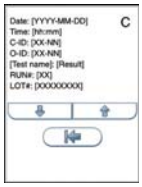
1

Main menu

Touch to enter patient results.

Touch to enter control results.

2



The last patient result or control is displayed.

To view more results touch or

If a printer is connected, touch to print the result.

Result records may be exported if a USB flash (FAT 32 formatted) is inserted into the Alere Afinion™ USB port.

Touch to export the results. The results will be stored on the USB in a .txt file for each assay tested on the Alere Afinion™ AS100 Analyzer. These files may be opened in e.g. Microsoft Excel for further processing.

	A	B	C	D	E	F	G	H	I	J	K	L
1	Test type	Serial number	Cartridge lot no	Patient ID	Patient ID 2	Patient ID 3	Patient ID 4	Operator ID	Test date	% HbA1c	mmol/mo	eAG
2	HbA1c	AS0007962	10125032	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130924 08:11	5.2 %		
3	HbA1c	AS0007962	10125113	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 08:29	3.1 %		
4	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 08:39	3.3 %		
5	HbA1c	AS0007962	10125032	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 09:50	8.2 %		
6	HbA1c	AS0007962	10125032	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 10:01	5.1 %		
7	HbA1c	AS0007962	10125113	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 11:23	5.3 %		
8	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 12:01	3.8 %		
9	HbA1c	AS0007962	10125113	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 13:20	3.3 %		
10	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 13:56	9.2 %		
11	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 14:01	5.1 %		
12	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 14:12	5.2 %		
13	HbA1c	AS0007962	10125032	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 15:04	6.1 %		
14	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 15:12	3.3 %		
15	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 15:25	8.2 %		
16	HbA1c	AS0007962	10125034	PATIENTID1	PATIENTID2	PATIENTID3	PATIENTID4	OPR0001	20130926 16:20	5.1 %		

Caution

⚠ When you export data that contains patient information, it is your responsibility to comply with your local regulations on protection of personal health information.

When an information code appears

Information codes that might appear during use of the Alere Afinion™ AS100 Analyzer refer to specific information messages. The code numbers, the possible causes and actions to take are listed below.

If the Analyzer detects a problem during processing of a Test Cartridge, the test will automatically be aborted and the Test Cartridge will be safely moved to the cartridge chamber. Proceed as follows:

1 

Record the code number (#) and touch ✓ to accept.

The lid opens automatically.

2 

Remove the Test Cartridge.

If the Test Cartridge is not ejected, restart the Analyzer.

Do not re-use the Test Cartridge.

3 

Look up the possible cause from the table below, and take actions to solve the problem.

If the problem persists, contact your local Alere Afinion™ supplier (see “Service information” page 29).

⚠ Do not re-use a Test Cartridge that has been rejected by the Analyzer. Collect a new sample and repeat the test with a new Test Cartridge.

Information codes caused by assay specific limitations

[#]	Cause	Action to take
103	Hemoglobin too low	Consult the Alere Afinion™ HbA1c Package Insert, section Test result reporting.
104	Hemoglobin too high	Consult the Alere Afinion™ HbA1c Package Insert, section Test result reporting.
105	HbA1c too low	Consult the Alere Afinion™ HbA1c Package Insert, section Test result reporting.
106	HbA1c too high	Consult the Alere Afinion™ HbA1c Package Insert, section Test result reporting.
107	Creatine too high	Consult the Alere Afinion™ ACR Package Insert.
108	Blood in urine	Consult the Alere Afinion™ ACR Package Insert.

Information codes caused by sample or Test Cartridge failure

[#]	Cause	Action to take
201	Insufficient sample volume: - Empty capillary - Air bubble in capillary - Capillary incompletely filled	Repeat the test with a new sample and Test Cartridge. Ensure that the capillary is completely filled with no air bubbles.
202	Excess sample on the sampling device exterior	Repeat the test with a new sample and Test Cartridge. Ensure that only the tip of the capillary is in contact with the sample.
203	Wrong sample material	Repeat the test with a new sample and Test Cartridge. Ensure that proper sample material is used (see Package Insert for the Alere Afinion™ test in use, section Specimen collection and storage).
204	Coagulated sample	Repeat the test with a new sample and Test Cartridge. The time from filling the capillary until analyzing the Test Cartridge should be as short as possible.
	Hemolysed blood sample or poor sample quality	Consult the Alere Afinion™ Package Insert. Repeat the test with a new sample and Test Cartridge.
	Test Cartridge or Analyzer failure	Repeat the test with a new sample and Test Cartridge. If the problem persists, restart the Analyzer and run controls.
205	Capillary cracked or damaged	Repeat the test with a new sample and Test Cartridge. Inspect the sampling device before use and handle with care.
206	Barcode label not readable (dirty or damaged)	Repeat the test with a new sample and Test Cartridge. If the problem persists, restart the Analyzer and run controls.
207	No sampling device inserted	Repeat the test with a new sample and Test Cartridge.
	Used sampling device belongs to another Alere Afinion™ test	Repeat the test with a new sample and Test Cartridge. Ensure that the sampling device and Test Cartridge have the same label color.
	Label on sampling device not readable (dirty or damaged)	Repeat the test with a new sample and Test Cartridge. Ensure that the label is clean.
208	Test Cartridge previously used	Repeat the test with a new sample and Test Cartridge.
209	Test Cartridge has passed expiration date	Check expiration date on the Cartridge pouch or box. Repeat the test using a new sample and a new Test Cartridge from another lot.
	The date in the Analyzer is incorrectly set	Check the date in the Analyzer to make sure it is set correctly. Repeat the test with a new sample and Test Cartridge.
210	Test Cartridge temperature too low	Repeat the test with a new sample and a new Test Cartridge within recommended operating temperature range (see Package Insert for the Alere Afinion™ test in use).
211	Test Cartridge temperature too high	Repeat the test with a new sample and a new Test Cartridge within recommended operating temperature range (see Package Insert for the Alere Afinion™ test in use, section Test procedure).
212	Software upgrade is required to run this test	Contact your local supplier for assistance.
	The Analyzer is configured for CLIA waived tests only	See CLIA Statements on page 2 for further information. Contact your local supplier for assistance.
213 **214**	Test Cartridge or Analyzer failure	Repeat the test with a new sample and Test Cartridge. If the problem persists, restart the Analyzer and run controls.
215	Test Cartridge or Analyzer failure	Repeat the test with a new sample and Test Cartridge. If the problem persists, restart the Analyzer and run controls.
	Hemolysed blood sample or poor sample quality (Alere Afinion™ HbA1c)	Consult the Alere Afinion™ HbA1c Package Insert. Repeat the test with a new sample and Test Cartridge.
217	Hemolysed blood sample or poor sample quality (Alere Afinion™ HbA1c)	Consult the Alere Afinion™ HbA1c Package Insert. Repeat the test with a new sample and Test Cartridge.
218	Condensation detected on cartridge	Run a new test cartridge, ensure that the cartridge is equilibrated to room temperature before the foil pouch is opened.

Information codes or messages caused by Analyzer failure

[#]	Cause	Action to take
301	Self-test failed	Restart the Analyzer.
302	Analyzer failure	Restart the Analyzer and run controls. Repeat the test with a new sample and Test Cartridge.
303	Analyzer temperature is too high	Ensure that the operating temperature is within recommended range (15-32°C, 59-89°F). Wait until the Analyzer has cooled down. Repeat the test with a new sample and Test Cartridge.

304	Analyzer temperature is too low	Ensure that the operating temperature is within recommended range for the Alere Afinion™ test in use (see Package Insert). The Analyzer temperature is displayed in the Start-Up menu (see page 13). Repeat the test with a new sample and Test Cartridge.
305	- Printer improperly connected - Malfunction of the printer	Power off the Analyzer, reconnect the printer and restart the Analyzer. If the message persists, see the printer User Manual.

[#]	Cause	Action to take
Touch screen error	Touch screen failure/ Touch screen buttons do not respond accurately	Restart instrument and realign screen. If the problem persists, contact your local Alere Afinion™ distributor.
27 **28** **29**	Start-up procedure failed	Contact your local Alere Afinion™ supplier for assistance.
Self-test error. Analyzer in non-operative mode	Analyzer failure	Restart analyzer. If the problem persists, contact your local Alere Afinion™ supplier.

Other information codes

[#]	Cause	Action to take
401	No registered supervisors in operator list	At least one supervisor is required in the operator list when the instrument is configured to operator ID verified (see page 14 and 15)
402	Cannot delete last supervisor	At least one supervisor is required in the operator list when the instrument is configured to operator ID verified (see page 14 and 15).
403	This assay type is not accessible to the operator	The operator logged in does not have access to run this assay type. Please contact your supervisor.
404	Operator ID is not found in operator list	When configured to required the operator ID entered is required to be present in the operator list. Please contact your supervisor.

[#]	Cause	Action to take
501	The control lot has passed expiry date	Check the expiry date on the control lot package insert or kit box. Repeat the test using a sample for a new control lot.
502	Alere Afinion™ Control Data is not recoginzed and is not stored in control lot database	Re-enter the Alere Afinion™ Control Data (see page 17).
503	Control verificaton aborted.	The Alere Afinion™ Control Data entered was not recognized. The control test was aborted by the operator. Test result was not stored. Run new control test to reset QC lockout interval.
504	Required control test interval has expired. Patient testing is disabled for this assay.	A passed control run must be performed according to configuration to unlock this assay for patient testing.

[#]	Cause	Action to take
601	Operator list or control lot database is full	The operator list can store 500 operators and the control lot database can store 100 control lots. Delete an operator or control lot to enter a new item

Service information

The laboratory must notify the manufacturer of this test system of any performance, perceived or validated, that does not meet the performance specifications as outlined in the instructions.
The manufacturer provides a toll free line for technical support.
1.866.216.9505
The toll free number is available for use only in the United States of America.

Before asking for assistance, please record the following information:
- Alere Afinion™ AS100 Analyzer serial number (SN) – see page 1
- Software version number – see page 1 or start-up menu
- Alere Afinion™ test type
- Test Cartridge lot number – see foil pouch or kit container
- Control name and lot number – see vial label
- Control results obtained
- Description of the problem with reference to information codes or messages

Cleaning and maintenance

No maintenance of the Alere Afinion™ AS100 Analyzer is required other than cleaning the exterior and cartridge chamber.

Cleaning the exterior

Cleaning the exterior of the Alere Afinion™ AS100 Analyzer should be performed whenever necessary. Most spills and stains can be removed with water or a mild detergent.

- Power off the Analyzer. Unplug the power supply when the shut down procedure is completed.
- Clean the outside of the Analyzer and the touch display with a clean, lint-free and non-abrasive cloth dampened in water or a mild detergent.
- To *disinfect* the exterior of the instrument, first remove as much as possible of the spilled material with a cloth dampened in the disinfectant (2% glutaraldehyde or 0.5% sodium hypochlorite). The surface of the Analyzer should be exposed to the disinfectant for at least 10 minutes.[1]
- Allow the Analyzer to air dry.
- Plug in the power supply and power on the Analyzer.

- The Analyzer must be powered off and unplugged before cleaning.
- Do not use any cleaning liquid or equipment other than those recommended above.
- Do not immerse the Analyzer in water or other liquids.

Cleaning the cartridge chamber

The Alere Afinion™ AS100 Analyzer Cleaning Kit (REF 1116048) should always be used for cleaning the cartridge chamber.

The cartridge chamber should be cleaned immediately if materials or liquids are spilled in the cartridge chamber.
For regular maintenance (removal of dust particles etc.), the cartridge chamber should be cleaned every 30 days.

- Touch  to open the lid.
- Unplug the power supply.
- Wet a Cleaning Swab with 3 drops of water or a disinfectant (2% glutaraldehyde or 0.5% sodium hypochlorite). Do not soak.
- Carefully remove spills and particles from the cartridge chamber using the moistened swab.
- To disinfect the cartridge chamber, the surface of the chamber should be exposed to the disinfectant for at least 10 minutes.[1]
- Wipe off any residual liquid from the cartridge chamber using a new, dry Cleaning Swab.
- Close the lid.
- Plug in the power supply and power on the Analyzer.

- The Analyzer must be unplugged before cleaning.
- Do not use any cleaning liquid or equipment other than those recommended above.
- Do not allow liquid to drip off the Cleaning Swab into the Analyzer. If liquid drips into the Analyzer, optics can be destroyed.
- Do not immerse the Analyzer in water or other liquids.
- Do not move or tilt the Analyzer when cleaning the cartridge chamber.

Disposal of the Analyzer

For correct disposal according to the Directive 2012/19/EU (WEEE), contact your local Alere Afinion™ supplier.

Software upgrade

Consult the Alere Afinion™ AS100 Analyzer SW Upgrade Package Insert.

[1] Clinical and Laboratory Standards Institute (CLSI) Guideline M29-A3: "Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline - Third Edition". ISBN 1-56-238-567-4

Warranty

Alere Technologies AS warrants solely to the Buyer that the Alere Afinion™ AS100 Analyzer will be free from defects in materials and workmanship, when given normal, proper and intended usage, and will perform in accordance with Alere Technologies AS's specifications for a period of twelve months from the date of delivery.

At its expense, Alere Technologies AS agrees to repair, or at Alere Technologies AS's option, replace with a new or reconditioned unit, any Alere Afinion™ AS100 Analyzer which is under warranty and not performing substantially in accordance with applicable product specifications, provided that the Buyer has given Alere Technologies AS notification of such warranty claim within the warranty period. If Alere Technologies AS is unable after reasonable efforts to repair or replace the Alere Afinion™ AS100 Analyzer not performing substantially in accordance with applicable product specifications, the Buyer's sole remedy shall be the refund of an amount not to exceed the actual purchase price paid by the Buyer for the Alere Afinion™ AS100 Analyzer. All repairs will be done during normal working hours. All replaced parts shall become Alere Technologies AS's property. Alere Technologies AS may require the Buyer to ship the Alere Afinion™ AS100 Analyzer to Alere Technologies AS or elsewhere at Alere Technologies AS's expense, for warranty service to be performed.

Notwithstanding the foregoing, Alere Technologies AS shall have no obligation to make repairs, replacements or corrections which result, in whole or in part, from (i) an act of God or other unforeseen catastrophe, (ii) any error, omission or negligence of the Buyer, (iii) improper or unauthorized use of the Alere Afinion™ AS100 Analyzer, (iv) operating errors or the disregard of warnings and precautions described in this Alere Afinion™ AS100 Analyzer User Manual; (v) repairs performed to the Alere Afinion™ AS100 Analyzer by any person other than an authorized Alere Technologies AS service representative; (vi) use of the Alere Afinion™ AS100 Analyzer in a manner for which it was not designed, (vii) causes external to the Alere Afinion™ AS100 Analyzer such as, but not limited to, power failure or electric power surges, or (viii) use of the Alere Afinion™ AS100 Analyzer in combination with equipment, components or software not supplied by Alere Technologies AS.

EXCEPT AS STATED IN THIS SECTION OF THE USER MANUAL, ALERE TECHNOLOGIES AS DISCLAIMS ALL WARRANTIES, WHETHER EXPRESS OR IMPLIED, WRITTEN OR ORAL, WITH RESPECT TO THE ALERE AFINION™ AS100 ANALYZER, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. ALERE TECHNOLOGIES AS'S MAXIMUM LIABILITY ARISING OUT OF THE SALE OF THE ALERE AFINION™ AS100 ANALYZER OR ITS USE, WHETHER BASED UPON WARRANTY, CONTRACT, TORT OR OTHERWISE, SHALL NOT EXCEED THE ACTUAL PURCHASE PRICE PAID BY THE BUYER FOR THE ALERE AFINION™ AS100 ANALYZER. IN NO EVENT SHALL ALERE TECHNOLOGIES AS BE LIABLE FOR SPECIAL, INCIDENTAL OR CONSEQUENTIAL DAMAGES, INCLUDING, BUT NOT LIMITED TO, LOSS OF PROFITS, LOSS OF DATA OR LOSS OF USE DAMAGES, ARISING HEREUNDER OR FROM THE SALE OF THE ALERE AFINION™ AS100 ANALYZER. THIS WARRANTY MAY NOT BE TRANSFERRED BY THE BUYER.

The acknowledgement of claims shall be reported to your Technical Care Specialist at 1.866.216.9505

Alere Afinion™ AS100 Analyzer

Analyzer	
Size	13,4 x 6,7 x 7,4 in. / 340 x 170 x 190 mm
Weight	11 lbs. / 5 kg
Display	Standard LCD color display with back light and integrated touch panel. Resolution: 240 x 320 pixels. Visible area: 2.3 x 3.0 in. / 58 x 77 mm.
Camera	640 x 480 pixels
Capacity of result records	500 patient results and 500 control results
Capacity of operator list	500 operators
Capacity of control lot database	100 control lots
SW update	via USB flash drive
Communication interface	RS 232C, USB 1.1
Power supply	
Power cord adapter	Separate AC to DC power cord adapter. Double insulated.
Input	100-240 VAC, 50/60 Hz, 42 W
Output	24 VDC ± 5%, 1.75A
Output connector	0.2 x 0.1 in. / 5.5 x 2.5 mm plug. Positive (+) on inner pin.
Adapter standards	IEC/EN-60950/UL 1950 (USA and Europe). EN-60601/UL 2601 (Japan). Approved for in vitro diagnostic medical devices.
Operating conditions	
Temperature	15-32ºC (59-89ºF)
Relative humidity	10-90%, non-condensing
Location	Dry, clean, horizontal surface. Avoid direct sunlight.
Test Cartridge temperature	According to specifications for the Alere Afinion™ test in use.
Storage and transport (in the original container)	
Temperature	-40 to 70ºC (-40 to 158ºF)
Relative humidity	10-93% at 40ºC (104ºF)

Additional equipment

For information regarding recommended barcode reader, printer, The Alere Afinion™ AS100 Analyzer Cleaning Kit, USB flash drive or Alere Afinion™ Data Connectivity Converter, please call 1.866.216.9505.

The touch buttons and their function

Touching a button on the screen will activate the function of this button. All the touch buttons that may appear during operation of the Alere Afinion™ AS100 Analyzer are explained below by their function.

Menu	Touch button	Name	Function
Start-up menu		Patient sample mode	Select patient sample mode.
		Control mode	Select control mode.
		Main menu	Enter main menu (operator ID, patient records, control records and configuration menu).
		QC lockout status	Enabled-unlocked All controls are within the configured interval. It is possible to run patient tests for all assays.
		QC lockout status	Warning-unlocked All controls are within the configured interval. When one or more of the assays has 10 % or less of the configured interval remaining the warning icon will be displayed. It is possible to run patient tests for all assays.
		QC lockout status	Expired-locked One or more controls have expired according to the configured interval. Patient testing on the expired assay has been locked.
		Operator logout button	Manual operator logout button.
Main menu		Patient records	View patient result records. View, print or export patient results.
		Control records	View control result records. View, print or export control results.
		Configuration menu	Enter configuration menu (language, patient ID on/off, date/time and screen/volume).
Configuration menu		Patient ID configuration	Configure patient ID function.
		Operator menu	Configure operator function.
		Language	Enter language selection.
		Screen/Beeper volume menu	Configure screen and beeper volume settings (screen contrast, screen adjustment and beeper volume).
		Date/Time menu	Enter date/time settings (date and time).
		QC lockout menu	Configure QC lockout function.
		General settings	Enter the general settings menu.
Patient ID menu		Patient ID disabled	Patient ID disabled.
		Patient ID enabled	Patient ID enabled and required.
Operator menu		Operator ID configuration	Configure operator ID function.
		Automatic operator logout	Configure number of minutes before automatic logout of operator.
		Operator list	Manage operator list. View, add, edit and delete operators.
Patient and control records		Print	Print result on connected printer.
		Result records export	Export result records to connected USB flash.
Universal buttons		Patient ID	Enter patient ID.
		Control ID	Enter control ID.
		Enter	Enter and return to previous view.
		Backspace	Delete previous character.
		Increase	Increase contrast/volume.

Menu	Touch button	Name	Function
		Decrease	Decrease contrast/volume.
		Scroll up	View previous
		Scroll down	View next
		Exit	Exit current menu and return to previous screen view.
		Accept	Accept (a setting or a test result).
		Abort	Abort the test result or cancel operation.
		Add button	Add new operator or control lot.
		Delete button	Delete operator or control lot.
		Edit button	Edit QC lockout interval or operator ID.
Operator ID configuration		Operator ID disabled	Operator ID function is disabled.
		Operator ID enabled	Operator ID is required to be entered to run an Alere Afinion™ Test Cartridge
		Operator ID enabled with verification	Operator ID is required to be entered to run an Alere Afinion™ Test Cartridge. The operator ID is verified against the instrument operator list.
Screen/Beeper volume menu		Screen contrast	Enter screen contrast setting.
		Screen alignment	Enter screen alignment function.
		Beeper volume	Enter beeper volume setting.
Date/Time menu		Date	Enter date setting.
		Time	Enter time setting.
General settings menu		Erase	Erase all content and configurations.
QC lockout menu		QC lockout	Enable/disable QC lockout function.
		QC lockout interval	Configure QC warning and lockout interval.
		Control lot information	View, add or delete control lots stored on instrument.
Operator list		Operator list export	Export operator list from instrument to USB flash.
		Operator list import	Import operator list from USB flash to instrument.
QC lockout		QC lockout disabled	QC lockout is disabled for this test.
		QC lockout enabled	One passed control run of either C I or C II is required to reset QC lockout interval.
		QC lockout enabled	Two passed control runs, C I and C II is required to reset QC lockout interval.
QC lockout interval		Interval by number of patient tests	QC reminder and lockout active after a configured set of patient tests.
		Interval by number of hours	QC reminder and lockout active after a configured set of hours.

Other symbols and signs

Other symbols, signs and abbreviations that may appear during operation of the Alere Afinion™AS100 Analyzer are explained below. These symbols or signs are only informative and can not be activated like the buttons.

Symbol	Meaning	Appears when?
	Wait!	Hour-glass icon that appears in the start-up procedure.
 [#]	Information code	Icon used along with a code number [#] that corresponds to code specific information messages [#] (see “Information codes and troubleshooting”).
	Operator ID	Icon illustrates the operator ID.
	Patient ID	Icon illustrates the patient ID.
	Control ID	Icon illustrates the control ID.
✓	Quality control pass	Control result is within acceptable range.
✗	Quality control failed	Control result is outside acceptable range.
↑	Result is above acceptable range	The displayed control result is above acceptable range.
↓	Result is below acceptable range	The displayed control result is below acceptable range.
C	Control	The letter C will appear on the screen when the control mode is selected.
O-ID	Operator ID	Abbreviation used in the patient and control records.
P-ID	Patient ID	Abbreviation used in the patient records.
C-ID	Control ID	Abbreviation used in the control records.
RUN#	Run number	Abbreviation used in the patient and control records for the run number of the analysis. This numbering is reset each day at midnight.
LOT#	Lot number	Abbreviation used in the patient and control records for the lot number of the Test Cartridge.
USER	User	Operator with user privileges.
SUPERVISOR	Supervisor	Operator with supervisor privileges.

The following symbols and abbreviations are used in the product labelling and instructions for the Alere Afinion™ AS100 Analyzer System.

Symbol/Abbreviation	Explanation
CE	Conformity to the European directive 98/79/EC on in vitro diagnostic medical devices
IVD	*In Vitro* Diagnostic Medical Device
REF	Catalog number
LOT	Lot number
SN	Serial number
TEST CARTRIDGE	Test Cartridge
CONTROL C I	Control C I
CONTROL C II	Control C II
CLEANING KIT	Cleaning kit
	Waste Electrical and Electronic Equipment (WEEE)
	Contents sufficient for "Σ" number of tests
	Expiry date (year-month)
	Storage temperature limitations
	Manufacturer
	Fragile, handle with care
	Keep away from sunlight
	Keep dry
	Operator's handling
	Warnings and precautions
	Consult the Alere Afinion™ user instructions
	Direct current
	USB port
IOIOI	Serial port
	Double insulation
LED	Light Emitting Diode
PC	Personal Computer
ID	Identification
HIS	Hospital Information System
LIS	Laboratory Information System
LCD	Liquid Crystal Display
AC	Alternating Current
DC	Direct Current

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