

FDA Executive Summary – Appendices

July 22, 2016

Clinical Chemistry and Clinical Toxicology Devices Panel

k153726

Afinion HbA1c Dx test system

Alere Technologies AS

Appendix A:

2016 American Diabetes Association “Standards of Care of Diabetes” Guidelines

Appendix B:

Proposed Labeling Afinion HbA1c Dx

Appendix C:

Agency review of diagnostic HbA1c devices

Appendix A: 2016 “Standards of Care of Diabetes” ADA Guidelines

Please see next page.

Diabetes Care[®]

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JANUARY 2016

SUPPLEMENT
1

AMERICAN DIABETES ASSOCIATION

STANDARDS OF MEDICAL CARE IN DIABETES—2016

American Diabetes Association
**Standards of
Medical Care in
Diabetes—2016**



Appendix B: Proposed Labeling Afinion HbA1c Dx

Please see next page.



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

XXXXXXXX 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 glycohemoglobin¹.

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 diabetes².

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.

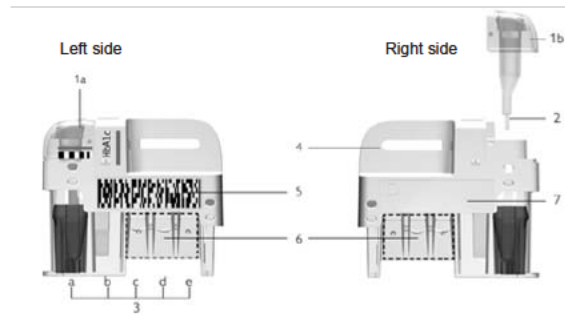


Figure 1 Alere Afinion™ HbA1c Dx Test Cartridge.

| 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 (59-77°F)

- 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=ethylenediamine 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.

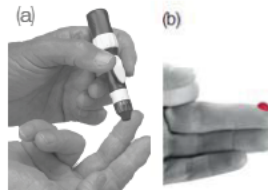
Important!

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.

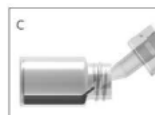
Sampling from a tube

- 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 (18-30°C, 64-86°F) 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 glycosylated 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 glycosylated 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 1 diabetes, 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/Na₂-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





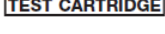







The precision of the Alere Afinion™ HbA1c Control was assessed at three study sites. Each site tested the two levels of controls: Control C I and Control C II. Three lots of Alere Afinion HbA1c Dx were used at each of the three study sites. The controls were analyzed in quadruplicate on each of the three 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.

| | |
|---|---|
|  | Conformity to the European directive 98/79/EC on <i>in vitro</i> diagnostic medical devices |
|  | <i>In vitro</i> Diagnostic Medical Device |
|  | Catalog number |
|  | Lot number |
|  | Test Cartridge |
|  | Contents are sufficient for one test |
|  | Contents sufficient for 15 tests |
|  | Consult instructions for use |
|  | Warnings and precautions |
|  | Expiration date (year-month) |
|  | 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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www.alere.com

ISO 13485 certified company.

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XXXXXX Rev. A 20XX/XX

AREA
WITHOUT
VARNISH

Alere Afinion™ HbA1c Dx

REF 111XXXX

For reordering please contact
1-877-441-7440

Technical Support
1-866-216-9505

Alere Technologies AS
Kjellerveien 101
PO Box 100
NO-2007 Oslo, Norway

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111XXXX Rev. A 2016/11



Alere Afinion™ HbA1c Dx



AREA
WITHOUT
VARNISH



Placed at room temperature (date):

New expiry date:

Hemoglobin A1c test kit

Intended use:
For determination of hemoglobin A1c 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

Contents:

- 15 Test Cartridges
- 1 Package Insert

REF 111XXXX
 LOT 12345678
 Int. 2016-01-28
 987654321



69 0600123456789
PRMMD (17)

AREA
WITHOUT
VARNISH

REF 111XXXX

Alere Afinion™ HbA1c Dx



AREA
WITHOUT
VARNISH

| | | |
|--|--|---|
| Alere Afinion™ HbA1c Dx US Box, 15 Test | | |
| PMS 229C Cariberry Black | PMS 347 Green Non Varnish Area | PN: 111XXXX Rev: A Date of Last Revision: A.1 2015/11 |

CLIA statement

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

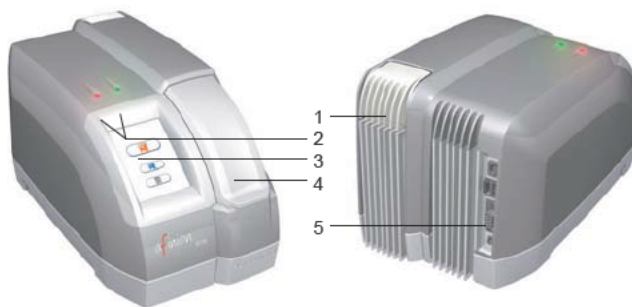
Important!

- 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.



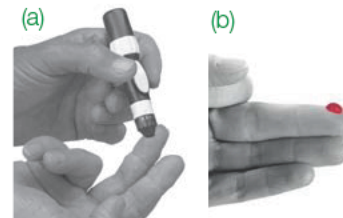
3 Procedure for Collecting the Sample

Sampling from a Control Vial

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

Sampling from Finger

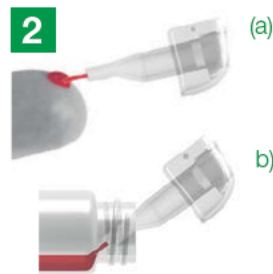
- Always use gloves.
- Cleanse the finger using alcohol. Allow the area to air dry.
- Use a lancet and firmly prick the finger (a). Properly dispose the lancet.
- Allow a good drop of blood to form before sampling (b).
- Apply direct pressure to the wound site with a clean gauze pad.



Specimen Collection using the Alere Afinion™ HbA1c Dx Test Cartridge



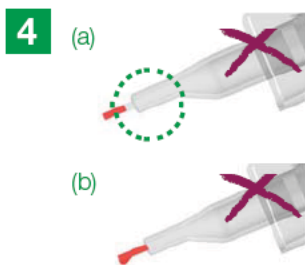
Pull up the sampling device.



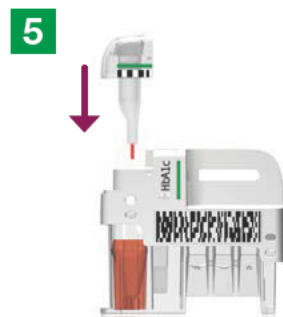
Touch the surface of the blood drop (a) or control (b).



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



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



Insert the sampling device immediately.



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.



alere.com

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NO-0504 Oslo, Norway



Alere Afinion™ AS100 Analyzer

US

REF 1115175/1115390, 111XXXX

CE

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.

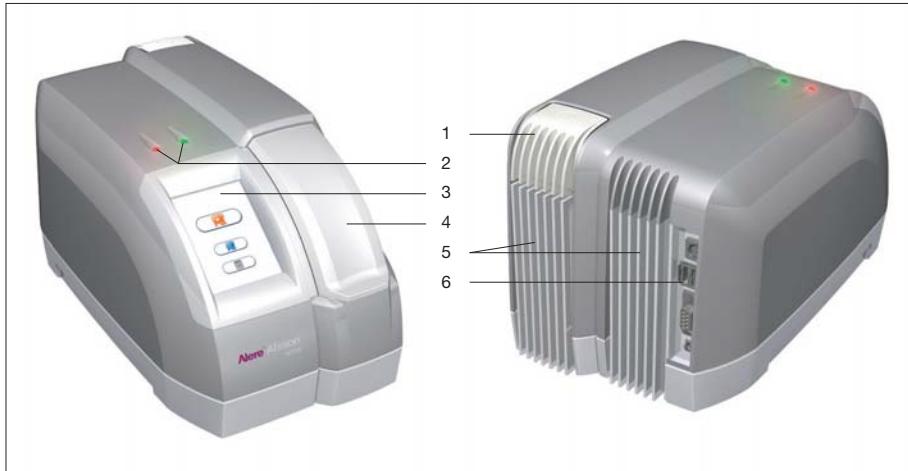


Figure 1

- | | |
|-----------------------|--|
| 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:

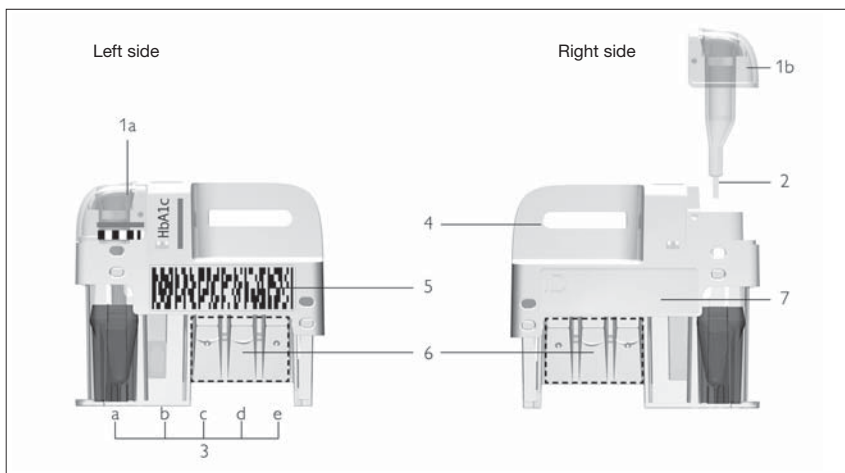


Figure 2

- | | | |
|---|-----------------------|--|
| 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 (Figure 1). 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)

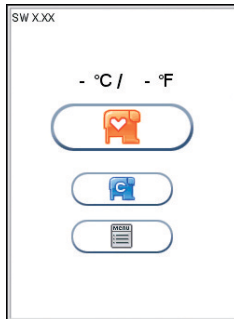
The red diode is illuminated when the Analyzer is busy. A flashing red light is seen when an information code is displayed. The green diode is illuminated when the Analyzer is ready for use. A flashing green light indicates completion of an analysis.

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

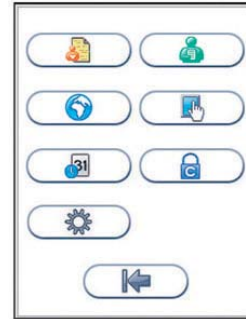
Start-up menu



Main menu



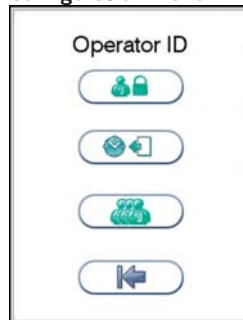
Configuration menu



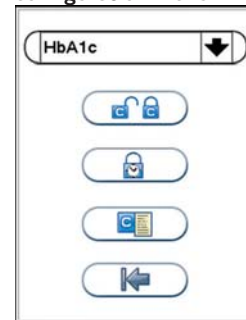
Patient ID configuration menu



Operator configuration menu



QC lockout configuration menu



Language settings



Date/Time Menu







Screen and beeper volume menu

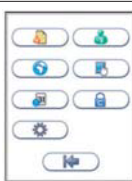


Setting the configuration

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

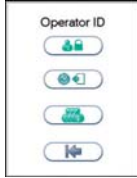
The patient identification (ID) function can be enabled or disabled. The patient ID function is enabled as a default setting by the manufacturer. When the patient ID function is enabled, the patient ID must be entered for each Test Cartridge to be analyzed. If the patient ID function is disabled, a run 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.

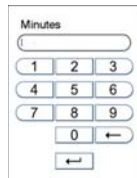



- Select  to disable the operator ID function.
- Select  to enable operator ID. Any operator ID is accepted.
- Select  to enable operator ID with verification.
 - To enable this function at least one supervisor is required to be present in the operator list.
 - When operator ID verified is enabled, instrument 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.






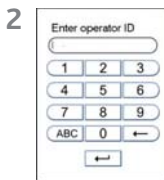
- Enter the number of minutes before automatic logout of operator.
- The operator will automatically be logged out after the configured number of minutes after analysis of the test is complete.
- Touch  to confirm and return to previous view.


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.

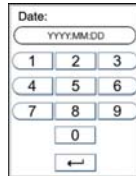
1



Touch to enter date setting.

Touch to enter time setting.


2






Enter today's date or time.

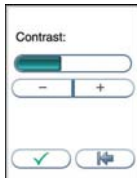
Touch to confirm and return to the previous view.




Adjusting screen/beeper volume settings

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



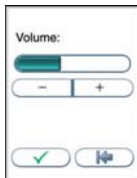
Touch  to enter the screen contrast setting.
Touch  to enter the screen alignment setting.
Touch  to enter the beeper volume setting.






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

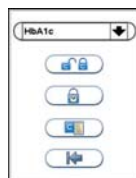
Touch  in the configuration menu to enter the general settings menu.






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

QC lockout configuration

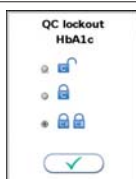
The QC lockout function is disabled as a default setting by the manufacturer.
 Touch  in the configuration menu to enter the QC lockout setting menu.







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  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 specific data:

- Alere Afinion™ control lot number
- Control expiry date
- Control type (assay)
- Acceptable control range
- Control level (C I or C II)
- 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 troubleshooting” 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: | | |
|---|--|--|
|  <p>1</p> |  <p>2</p> |  <p>3</p> |
| <p> Remove the sampling device from the Test Cartridge.</p> <p><i>Use the handle to keep the Test Cartridge steady against the table and pull the sampling device straight up.</i></p> | <p>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. <u>Do not</u> wipe off the capillary.</p> <p><i>Avoid air bubbles and excess sample on the outside of the capillary.</i></p> | <p>Immediately and carefully replace the sampling device into the Test Cartridge.</p> <p><i>The time from filling the capillary until analysing the Test Cartridge must be as short as possible.</i></p> |




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.

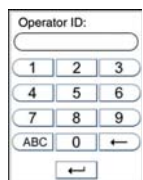
Using the operator ID function

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.

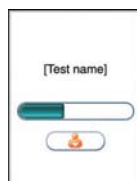
Using the patient ID function



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).

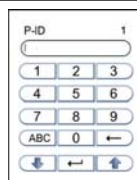
Entering patient ID

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.



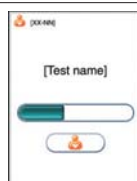
- 2 It is possible to enter up to four patient ID entries for each patient, P-ID 1 to 4. When enabled, P-ID 1 is required to be entered. Scrolling between the patient IDs is done with the  and .



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

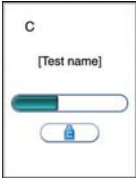
In quality control testing, a suitable control ID must always be entered. The lot number of the control material is recommended as a suitable control ID. The control ID function cannot be disabled.



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:

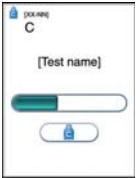
1 Touch  to enter the control ID option.



2 Enter control ID by numbers and/or touch  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

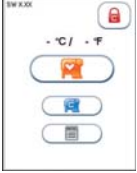

The status of the enabled QC lockouts is presented with a QC lockout status button (padlock symbol) visible in the Start-up menu. This gives the operator the status of QC lockout before he/she attempts to run any tests.

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

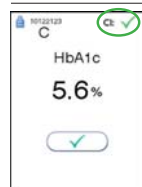
Remaining time (dd:hh:mm) or number of runs for each assay with active QC lockout is shown. dd is the number of days, hh is the number of hours, and mm is the number of minutes until the assay will be locked. # is number of patient tests.

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.

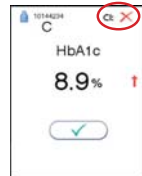


Passed (within the acceptable control range)

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  **c** 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 | Test Cartridge or Analyzer failure | Repeat the test with a new sample and Test Cartridge. |
| 214 | | 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 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 | 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 recognized and is not stored in control lot database | Re-enter the Alere Afinion™ Control Data (see page 17). |
| 503 | Control verification 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.

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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 | 15-32°C (59-89°F) |
| 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 70°C (-40 to 158°F) |
| Relative humidity | 10-93% at 40°C (104°F) |

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. |

GALLERY OF ICONS

| 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. |

SYMBOLS AND ABBREVIATIONS

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

| Symbol/Abbreviation | Explanation |
|---|--|
|  | Conformity to the European directive 98/79/EC on in vitro diagnostic medical devices |
|  | <i>In Vitro</i> Diagnostic Medical Device |
|  | Catalog number |
|  | Lot number |
|  | Serial number |
|  | Test Cartridge |
|  | Control C I |
|  | Control C II |
|  | 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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Appendix C: Agency review of diagnostic HbA1c devices

For monitoring patients with diabetes, clinicians generally interpret a difference of 0.5% HbA1c between successive patient samples as a significant change in glycemic control (Weykamp C, 2013; Leters-Westra E 2014b). For diagnostic purposes, the margins of clinical decision limits for HbA1c distinguishing between a normal, pre-diabetes, or diabetes diagnosis are also quite narrow (see section II). Therefore, it is critical that HbA1c methods intended for use as an aid in the diagnosis and/or risk assessment of diabetes are as accurate and precise as possible.

In 510(k) submissions for HbA1c test systems with a diagnostic intended use, sponsors must demonstrate substantial equivalence of their device with a legal predicate, which includes fulfilling the special controls requirements specific to 21 CFR 862.1373. During the pre-market review, FDA assesses the performance of diagnostic HbA1c devices in the following areas:

1. Precision

Sponsors must demonstrate repeatability (within-run) and reproducibility (between-run, between-day, between-instrument) imprecision in blood samples containing approximately 5.0%, 6.5%, 8.0%, and 12% HbA1c. This testing must evaluate precision over a minimum of 20 days. At least three lots of reagents should be evaluated on each of at least three instruments.

2. Linearity

Sponsors should demonstrate that their device generates linear results across the claimed measuring range of the device.

3. Traceability

Sponsors must demonstrate initial and annual standardization verification by a glycohemoglobin standardization certification program, such as NGSP. The NGSP certification process evaluates agreement of each method using one lot of reagents and calibrators, one instrument, and one application on venous whole blood samples under optimized testing conditions.

4. Limit of Detection

Sponsors should demonstrate the Limit of Blank (i.e., signal “noise” generated in a blank sample), Limit of Detection, and Limit of Quantification (i.e., the lowest concentration that can be quantified) for their assay.

5. Analytical Specificity

a. *Exogenous and endogenous interference*

Sponsors should demonstrate whether or not there are any endogenous substances (e.g., triglycerides, etc.) or pharmaceutical compounds (e.g., metformin, etc.) that could interfere with their device and cause false test results if present in a blood sample. If applicable, the sponsor should also investigate the effect of hemolysis on test results.

b. *Cross reactivity with hemoglobin derivatives*

Sponsors should demonstrate whether or not there is any interference by acetylated hemoglobin, carbamylated hemoglobin, labile HbA1c, glycated albumin, HbA10, and HbA1a+b.

c. *Hemoglobin variant interference*

Sponsors 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. In addition, sponsors should also evaluate any possible interference by Hemoglobin F.

6. Accuracy

Sponsors must evaluate at least 120 blood samples spanning the claimed measuring range of the device and compare the results of their device to results obtained by a standardized test method. Results must demonstrate little or no bias compared to the standardized method and total error at 5.0%, 6.5%, 8.0%, and 12.0% HbA1c must be $\leq 6\%$. For example, if the true value of a blood sample (as determined by the standardized test method) is 6.5%, the device may be expected to return test results as low as 6.1% or as high as 6.9% and still be within the total error requirements. At 5.0%, the expected range would be 4.7-5.3%, at 8.0%, the expected range would be 7.5-8.5%, and at 12.0%, the expected range would be 11.3-12.7%.

7. Matrix comparison (if applicable)

Sponsors should demonstrate that all sample matrices (e.g., different anticoagulants in blood collection tubes) produce equivalent test results when used with their device. If capillary samples are claimed, more robust precision and accuracy studies on capillary samples are necessary to demonstrate that the pre-analytical and sample collection steps do not unacceptably increase total error.

8. Additional review considerations for POC diagnostic HbA1c devices

Compared to assays intended for use in central laboratories, FDA evaluates additional variables for assays intended to be used in POC settings. In particular, FDA expects sponsors to demonstrate acceptable precision and accuracy with minimal bias in the hands of the intended users. The user demographic and level of training necessary for these performance tests depends on the complexity of the POC settings claimed (see section V). Special considerations for precision and accuracy studies for POC devices include:

a. *Sample type*

Typically, POC HbA1c devices are formulated to assess venous whole blood samples. Some POC devices, like the Afinion HbA1c test system, also accept capillary fingerstick blood samples. These matrices may perform quite differently from each other as well as from the standardized comparator method. Therefore, sponsors should demonstrate that precision and accuracy in all matrices (venous whole blood and capillary fingerstick samples, as applicable) are within an acceptable margin of error.

b. *POC precision*

For a robust assessment of repeatability and reproducibility by the intended users, sponsors should conduct a separate POC precision study. Users with training/education levels comparable to the intended user population should perform testing of all applicable sample matrices at multiple (typically at least three) POC sites using multiple reagent lots and multiple instruments. The chosen POC sites should represent all areas where the device may be used.

c. *POC accuracy*

Sponsors should demonstrate that intended users can use their device to obtain accurate test results in a realistic POC environment. For POC HbA1c devices, sponsors typically provide accuracy data from at least three POC sites. The chosen POC sites should represent all areas where the device may be used.