P

Diabetes Management Technology

CLOVER® A1c®

Test Cartridge

INSTRUCTION FOR USE

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1. INTENDED USE

The **CLOVER A1c®** Test Cartridge, together with the **CLOVER A1c®** Analyzer, which are part of the **CLOVER A1c®** System provides a convenient method for measuring the percent concentration of hemoglobin A1c (HbA1c %)
In both capillary blood and venous whole blood. The measurement of hemoglobin A1c concentration is recommended For monitoring the average blood glucose levels, for long-term care of people with diabetes. The **CLOVER A1c®** Test Cartridge uses boronate affinity assay to separate the glycated hemoglobin fraction form the non glycated fraction.
The **CLOVER A1c®** System is intended to be used by professionals in laboratories, clinics and hospitals.

2. SUMMARY AND EXPLANATION

Diabetes Mellitus, which is one of the leading causes of adult kidney failure, blindness and amputation, is known to shorten the average life expectancy of a person up to 15 years. Studies like the Diabetes Control and Complications Trial[1](DCCT) and the United Kingdom Prospective Diabetes Study[2](UKPDS) showed that the improved glycemic control by lowering blood sugar level, reduces the risk and progression of the most serious complications of diabetes. The level of hemoglobin A1c is proportional to the level of glucose in the blood over a period of approximately two months[3], for this reason, hemoglobin A1c is accepted as an indicator of the mean daily blood glucose concentration over the preceding two months[4][5]. The American Diabetes Association(ADA) recommends measurement of hemoglobin A1c levels two to four times per year, less frequently in stable control patients, and more in unstable control patients[6]. Studies have shown that the clinical values obtained through regular measurement of hemoglobin A1c leads to changes in diabetes treatment and improvement of metabolic control as indicated by a lowering of hemoglobin A1c values[7][8].

3. PRINCIPLES OF PROCEDURE

The ***CLOVER A1c®*** system is a fully automated boronate affinity assay for the determination of the percentage of Hemoglobin A1c (HbA1c %) in whole blood.

The Test Cartridge is composed of a cartirdge and a reagent pack contain -ing the reagents necessary for the determination of hemoglobin A1c, with a sample collecting area for blood sample collection.

The reagent pack is pre-filled with reaction solution and washing solution. The reaction solution contains agents that lyse erythrocytes and bind hemo -globin specifically, as well as a boronate resin that binds cis-diols of glycated hemoglobin.

The blood sample(4uL) is collected at the sample collecting area of the reagent pack, then the reagent pack is inserted into the cartridge, where the blood is instantly lysed releasing the hemoglobin and the boronate resin binding the glycated hemoglobin.

The reagent pack containing the blood sample is inserted in ***CLOVER A1c®*** Analyzer (in which the cartridge has been placed). The cartridge is automatically rotated, placing the blood sample in the measuring zone. The total hemoglobin is photometrically measured by the diffused reflectance of the optical sensor composed of both a LED(Light Emitting Diode) and a PD(Photo Diode).

Then, assembled cartridge is rotated and the rinsing solution washes out non-glycated hemoglobin from the blood sample, enabling photomectical measurement of glycated hemoglobin.

The ratio of glycated Hemoglobin and total hemoglobin is calculated.

$$\text{HbA1c\%} = A \times \left[\frac{\text{HbA1c}}{\text{Total Hemoglobin}} \times 100 \right] + B$$

'HbA1c' and 'Total Hemoglobin' are values obtained from the ***CLOVER A1c®*** system. 'A' and 'B' are the slope and intercept factor to correct the value for the calibration standard of NGSP.
* NGSP : National Glycohemoglobin Standardization Program

4. TEST COMPONENTS

The ***CLOVER A1c®*** test cartridges are intended for use with the ***CLOVER A1c®*** Analyzer only.

CLOVER A1c® Test Cartridge REF INFHS02B

• 10ea Test Cartridges

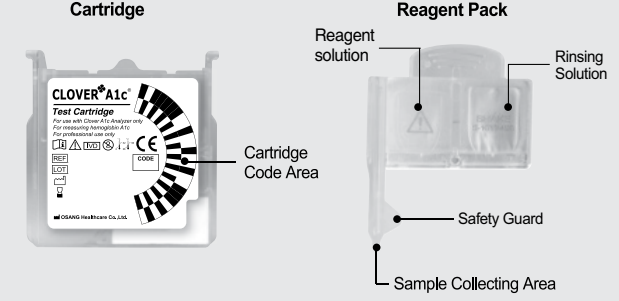
- Cartridge

- Reagent Pack : has 2 chambers to be inserted into the cartridge.

Chamber 1 (reagent solution) contains:
18 v/v % boronate affinity bead, surfactant, nonreactive ingredients, buffer.

Chamber 2 (rinsing solution) contains:
surfactant, nonreactive ingredients, buffer.

TEST CARTRIDGE



CAUTION: Do not touch the cartridge code area on the front or bead window at the back. Any contamination of these area may cause erroneous results.

Additional Items

• CLOVER A1c® Analyzer
• CLOVER A1c® Daily Check Cartridge
• CLOVER A1c® Monthly Check Cartridge
• Fan Filter
• Power Adapter
• PC Cable (optional)
• Thermal Printer (optional)
• Barcode Scanner (optional)

Additional Items needed for testing

• Sterile, single-use blood lancet
• Lancing device
• Disposable gloves
• Tissues, Cotton balls, Gauze

5. STORAGE AND USE

- Test Cartridge
Store test cartridge in the protective packaging until use.
The test cartridge is stable until the expiration date printed on the package when stored at 2-32℃ (36-90˚F). Do not freeze.

- Preparation of the Test Cartridge
Remove test cartridge from protective packaging.
If refrigerated, allow to reach room temperature for 30 minutes before use.
The operating temperature of the test is 17-32℃ (63-90˚F).

PRECAUTION/ WARNING:

- For professional use only.
- For in vitro diagnostic use only.
- If refrigerated, allow sealed pouches reach room temperature 30 minutes before use.
- Do not use test cartridge after expiry date on label, on pouch and box.
- Do not use scissors to open foil pouch, scissors may damage the reagent pack or cartridge.
- Handle and dispose of all samples and pipettes following appropriate biohazard procedures.
- Wear personal protective equipment while handling all reagents, samples, quality controls and while operating the CLOVER A1c® Analyzer.
- Waste material containing patient samples, quality controls or biological products should be considered bio hazardous at disposal or treatment.
- Do not touch the cartridge bead window.
- Disposal all waste in accordance with applicable national and/or local regulations.
- Use the test cartridge within 2 minutes after opening pouch.

6. PROCEDURE

Blood Sample

The capillary blood taken from a fingertip or venous blood collected in a tube with K_2 • K_3 EDTA, lithium heparin, sodium citrate or sodium fluoride/ oxalate as anticoagulants can be used for the ***CLOVER A1c®*** test.

Test Procedure

The ***CLOVER A1c®*** Analyzer setup is described in the ***CLOVER A1c®*** Analyzer Instruction for Use.

IMPORTANT : Please read through and familiarize yourself with the contents of this manual and the ***CLOVER A1c®*** System Instructions for Use before using the system.

STEP 1.

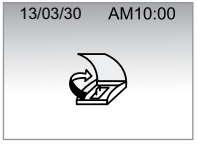
When the power is connected, the display shows 'Warming Up' until the device is ready for test.
Warming up will take approximately 5 minutes depending on the ambient temperature.

While warming, the ***CLOVER A1c®*** Analyzer performs hardware functionality test to verify that the internal optics and the mechanical system are operating correctly.

IMPORTANT : Do not move the analyzer during 'Warming up'.

STEP 2.

When 'Open the lid' is shown in stand-by mode, open the lid.



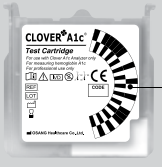
IMPORTANT : Regarding details on analyzer functionality, please refer to the anlayzer instruction for use.

STEP 3.

Tear the pouch open on the side with serrated edge.
Do not use scissors to open the pouch. Scissors may damage the reagent pack or cartridge.

Use the test cartridge within 2 minutes after opening the pouch.

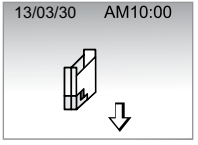
CAUTION: Do not touch the cartridge code area on the front or bead window at the back. Any contamination of these area may cause erroneous results.



STEP 4.

Gently insert the cartridge into the cartridge compartment when 'Insert Test Cartridge' is shown. Hold the cartridge with barcode facing left.

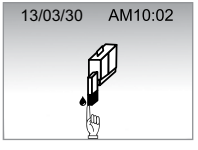
Ensure a gentle snap is either heard or felt to confirm proper placement.

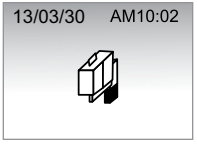


NOTE : Do not force the cartridge into the analyzer. It can only be placed in one way to fit. Environmental influences (e.g. air humidity and light) can damage the test cartridges and lead to false measurements or error messages.

STEP 5.

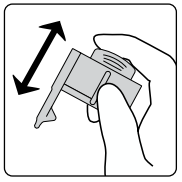
The display will show the 'Apply sample to sample area' and 'Insert Reagent Pack'.





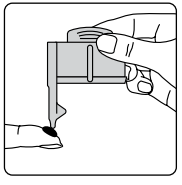
STEP 5-1.

Gently mix the reagent pack 5 ~ 6 times before applying blood sample.



CAUTION : Do mot mix it too vigorously to avoid air bubbles. If air bubbles appear, wait until they disappear before testing.

STEP 5-2.



Apply the blood sample at the sampling area by carefully touching the blood drop.
Ensure the sampling area is completely filled.

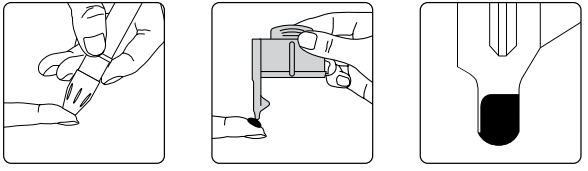
Once the reagent pack is filled with the blood sample, analysis must begin immediately.

Sample Collection and Handling

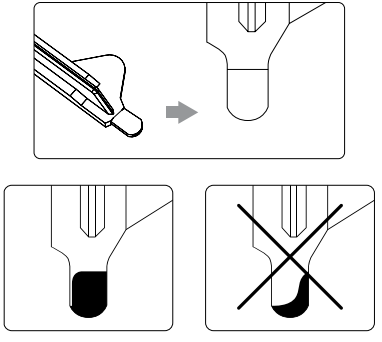
Capillary whole blood from fingertip and venous whole blood can be used for HbA1c testing. A 4μL blood sample is needed.

- Use of capillary blood

Puncture the fingertip to get minimum 4μL of capillary blood, touch the blood sample with the capillary tip of the Reagent Pack (sampling area). The blood is automatically drawn up. Ensure that the sampling area is completely filled.



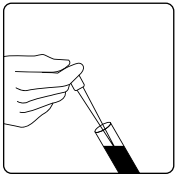
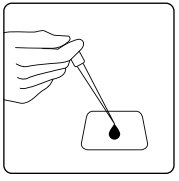
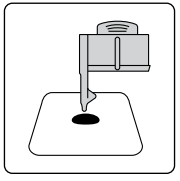
Reagent Pack Sampling Area.



IMPORTANT : Once the reagent pack is filled with the blood sample, analysis must begin immediately.

- Use of venous blood

Venous whole blood collected in tubes with K_2 • K_3 EDTA, lithium heparin, sodium citrate or sodium fluoride/ oxalate as anticoagulants can be used.
Venous whole blood can be stored at 2~8℃ for 7 days with unbroken seal (only 3 days when seal is broken) and at 20~25℃ for 3 days.
Allow blood samples to reach room temperature. Anti-coagulated blood should be mixed well prior to testing. Remove the stopper from the holder and take out a drop of blood sample on a clean container. Softly touch the sampling area of the reagent pack on the blood sample, and wait until the sampling area is completely filled.

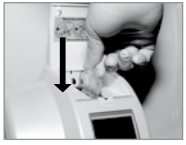
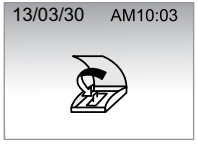
NOTE : Do not wipe off excess blood outside the sampling area. Do not touch the open end of the sampling area.

CAUTION : There is a potential risk of biological hazard. All parts of ***CLOVER A1c®*** System should be considered potentially infectious.

- **Use gloves.**
- **Dispose of used test cartridges in a sturdy container with lid.**
- **Consult local environmental authorities for proper disinfection procedures as well as disposal of consumables.**

STEP 6.

Insert the reagent pack into the cartridge compartment of the analyzer. The 'Close the lid' is shown.

NOTE : Do not force the reagent pack into the cartridge. It can only be placed in one way to fit.

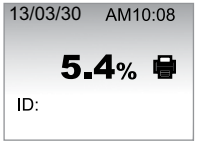
STEP 7.

The test starts automatically when the lid is closed.


IMPORTANT : Do not open the lid during testing.
Do not move the analyzer during testing.
Do not expose the analyzer to vibration during testing.

STEP 8.

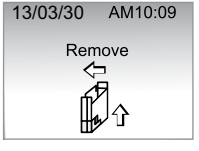
The measuring time is 5minutes and the test result will be displayed (in % or mmol/mol).



NOTE : If ">14%" or "<4%" displayed, please repeat test. If the second result also is out of the range, contact your local distributor for support.

STEP 9.

After the test is completed, open the analyzer lid. 'Remove cartridge' will be shown. Remove the test cartridge from the analyzer by gently pushing it to the left and pulling it out.



CAUTION : Do not force the cartridge from the analyzer. Dispose all waste in accordance with applicable national and/or local regulation.

Expected values

The American Diabetes Association's (ADA's) 2012 Clinical Practice Recommendation for diabetes specifies a treatment goal of less than 7% HbA1c.[6)]

Limitation of Procedure

The CLOVER A1c® assay gives accurate and precise results over a range of total Hemoglobin of 7 to 20 g/dL. Most patients will have hemoglobin concentrations within this range.
However, patients with severe anemia may have Hemoglobin concentrations lower than 7 g/dL, and patients with polycythemia may have Hemoglobin concentrations above 20 g/dL. Patients known to have these condition should be tested with another method for HbA1c determination.

7. QUALITY CONTROL

The ***CLOVER A1c®*** Check Cartridge checks the optical and operating systems of the Analyzer.

INPORTANT : Read through and familiarize yourself with the contents of the ***CLOVER A1c®*** Analyzer Instructions for Use before using the system.

- Type of Check Cartridges

- ***CLOVER A1c®*** Daily Check Cartridge
- ***CLOVER A1c®*** Monthly Check Cartridge

Storage Instruction

- The Check Cartridge must be protected from sunlight during storage; do not leave it in direct sunlight for longer periods of time.
- Store the Check Cartridge at 2-32℃ (36-90℉).
- Store the Check Cartridge at humidity < 90%.
- Always store the Check Cartridge in its protective packaging to prevent scraches which may affecting the result.
- If refrigerated allow Check Cartridge to reach room temperature for at least 1hour before use.

Precautions/Warning

- For In Vitro Diagnostic Use.
- Do not use the Check Cartridge beyond the expiration date printed on the Check Cartridge Label and Pouch.
- Do not use the Check Cartridge if it has been stored incorrectly, or if it is dirty, scratched or damaged in any way.

When to run the Check Cartridge

- Once a day before samples are tested. ***Daily***
- After the analyzer has been moved. ***Daily***
- If the test result is suspected incorrect. ***Monthly***
- After an error message. ***Daily & Monthly***
- Once a month before samples are tested. ***Monthly***

8. CALIBRATION

CLOVER A1c® **Analyzer:**
The ***CLOVER A1c®*** Analyzer is factory calibrated. The Analyzer automatically self-adjusts during each power-up and during each assay. An error message will appear if the analyzer is not able to make appropriate internal adjustments.

CLOVER A1c® **Test cartridge:**
At Test Cartridges production, each production lot undergoes a through analysis and characterization, before being released.
The ***CLOVER A1c®*** system test method is National Glycohemoglobin Standardization Program (NGSP) certified, thus the values of calibration parameters determined to provide an optimal reagent performance, are based on the Diabetes Control and Complications Trial (DCCT) reference method.
Calibration parameters are printed for each lot of Test Cartridges on the Test Cartridge label. As soon as the Test Cartridge is inserted into the analyzer, the system automatically recognizes the cartridge code. This accesses the appropriate calibration parameter values (calibration curve) for the particular lot number of reagent packs in use.

9. STANDARDIZATION

NGSP
The ***CLOVER A1c®*** Analyzer has been certified by the National Glycohemoglobin Standardization Program (NGSP). NGSP certifications are renewed annually. Current NGSP certifications are found on the web at:
http://www.ngsp.org/prog/index.html

IFCC
The relationship between HbA1c results form the NGSP network and the IFCC network has been evaluated and a master equation has been developed. IFCC results are consistently 1.5-2% HbA1c lower throughout the range of values compared to NGSP results[9].

IFCC value = [1.093 x NGSP value]-23.50

10. PERFORMANCE CHARACTERISTICS

Clinical Correlation

The system accuracy evaluation had been performed with 133 fresh venous and capillary blood samples, each with sufficient volume to be measured by two different analyzers and least in duplicate.
The percentage of HbA1c in clinical specimens ranging from **4%–14%** HbA1c (both venous and capillary) was determined to use the ***CLOVER A1c®*** system and ion exchange high performance liquid chromatography(HPLC) instrument.

Results are as follows:

Total				
Comparison type	**Regression line**	**Slope**	**y-intercept**	**R^2**
Reference vs. Total	y = 1.0157 x - 0.1088	1.0157	-0.1088	0.9877
Reference vs. Venous	y = 0.9972 x + 0.0495	0.9972	0.0495	0.9850
Reference vs. Capillary	y = 1.0127 x - 0.0889	1.0127	-0.0889	0.9918
Venous vs. Capillary	y = 0.9822 x + 0.1358	0.9822	0.1358	0.9843

Precision

Two whole blood samples, one of approximately 5% HbA1c (low), and one of approximately 9% HbA1c (high), were tested over 20 days in four runs per day, for a total of 80 assays per level. The overall imprecision (including within-day and between-day) was 2.7% CV at the low level and 2.1% CV at the high level.

Linearity and Temperature Effects

The ***CLOVER A1c®*** system has shown a linear response form 4%-14% HbA1c using patient samples at an operating temperature of 17-32℃.

Hemoglobin and Hematocrit

The ***CLOVER A1c®*** test performs acceptably over a hemoglobin range from 7-20g/dL and Hematocrit range of 20-60%.

Interference Testing / Specificity

Studies were performed to assess the effect of common interfering substances including various common over-the-counter therapeutic agents.
Two levels, 5.6 and 10.2 %HbA1c was tested. See table below.

INTERFERENT	TEST CONCENTRATION (mg/dL)
Acetaminophen	80
Bilirubin	40
Acetylsalicylic acid	70
Caffeine	30
Glyburide	0.19
Ascorbic acid	6
Hydroxyzine dihydrochloride	30
Triglyceride	3500
Urea	500

The above interferent, at the levels indicated, were shown to have no effect on the ***CLOVER A1c®*** System test results.

Effect of Hemoglobin Variants

Hemoglobin C, D, E, F and S

The hemoglobin (Hb) variant interference studies were performed using sample provided by NGSP. The sample contained the hemoglobin variants C, D, E, F and S.

Labile HbA1c

To study the interference from labile HbA1c on the assay, two whole blood samples representing normal and diabetic HbA1c levels were split into aliquots. The samples were incubated for three hours at 37 °C (99 °F) to facilitate formation of labile HbA1c. The labile HbA1c % in the samples were confirmed by the reference method Tosoh HLC-723 G7.

Hemoglobin C, D, E, F, S, and labile HbA1c do not significantly affect test results. However, abnormally high concentration in blood may cause inaccurately results. All tested Hb variants were shown to have no effect on the CLOVER A1c analyzer test results.

11. PRECAUTION

1. Analyzer should be located on the flat table.

2. CLOVER A1c® is a precise optical equipment. So, it should be installed in a stable place without vibration.

3. Electric power should be stable.

4. Analyzer and Cartridge are not to be exposed direct sunlight.

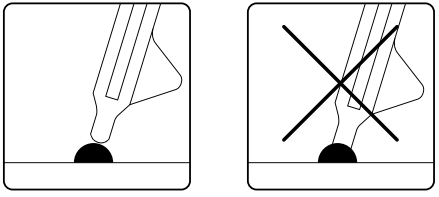
5. Users should carefully follow the indicated Analyzer operating tempera ture (17-32℃) and Cartridge storage temperature (2-32℃).

6. Allow the test cartridge and analyzer to reach room temperature (ambient temperature) 30 minutes before use.

7. Do not move or interfere with the analyzer during testing.

8. The bead inside the reagent solution of the Reagent Pack, might sink and coagulate. Mix the Reagent Pack before testing, and visually check that the beads are not coagulated.

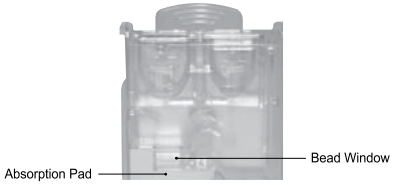
9. When collecting blood, touch the end of the capillary tip (sampling area) to the blood sample, do not put the tip deep into the blood sample to avoid excess blood.

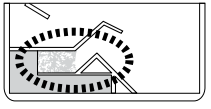


10. Do not apply too much pressure to the Reagent Pack when inserting it into the Cartridge. Insert the Reagent Pack gently. Much pressure may cause the mixture of the two reagents resulting in bad result.

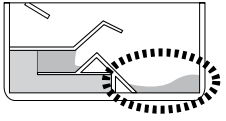
11. Firmly insert the reagent pack into cartridge with a mild pressure until tick sound form the cartridge.

12. After test completion and removal of cartridge, inspect the cartridge for symptoms. If any of the following symptoms occur, repeat the test to confirm validity of the result.

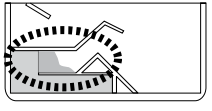




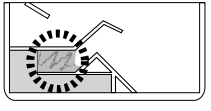
1) If the bead window is not colored uniformly.



2) If Reagent is left in the cartridge not be absorbed fully into Absorption Pad.



3) The bead window is only partly full.



4) If the cartridge has residue or some scratch on the bead window.

13. Besides, when any kind of errors happen as specified in the manual, refer to the troubleshooting instructions from the Analyzer instructions for use.

Symbol	Description
CE	This symbol indicates that this product complies with the requirements of Directive 98/79/EC on in vitro diagnostic medical device
	Consult Instructions for use
	Use By
	Caution, consult accompanying documents
IVD	In vitro diagnostic medical device
LOT	Batch Code
REF	Catalogue number
	Temperature Limitation
	Do not Reuse
	Date of Manufacture
SN	Serial Number
EC REP	Authorized representative in the European Community
	Manufacturer
	Keep away from sunlight
	Biohazard

REFERENCES

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132, Anyangcheondong-ro, Dongan-gu,
Anyang-si, Gyeonggi-do, Korea (14040)
www.osanghc.com

EC REP **Obelis S.A**
Bd.General Wahis 53,
1030 Brussels, Belgium
Tel : +(32) 2.732.59.54
Fax : +(32) 2.732.60.03
E-Mail : mail@obelis.net

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