skyla™ Hi
Hemoglobin A1c reagent kit

IVD

CE 0197

Product Code：801-100B

Suitable for Self-testing **Rev：C**

========== **Be sure to read and follow the instructions before use** ==========

1. Intended Use

The skyla™ Hi Hemoglobin A1c Reagent kit is an immunoassay used with skyla™ Hi Analyzer provides quantitative measurement of the percent concentration of glycated hemoglobin (%HbA1c) in both of capillary blood taken from the finger-prick, and venous whole blood. The use of this reagent kit is for users in healthcare institutions (e.g. clinic, laboratory, pharmacies and hospital). The measurements are used for monitoring of long-term efficacy of metabolic control in person with diabetes mellitus.

Precaution/Warning

1. This product is for in vitro diagnostic use only
2. The product must not be used individually for diagnostic purpose.
3. Please wear the gloves when performing the test.
4. Do not re-use any part of the test kit.
5. Dispose all waste in accordance with applicable national and/or local regulations.

2. Overview and Description

Glycated hemoglobin is hemoglobin A at the N terminal of the beta chain, formed through non-enzymatic glycation. The concentration of glycated hemoglobin is proportional to the glucose concentration in the blood over the past two months. Therefore, glycated hemoglobin can serve as an indicator of the long-term blood sugar

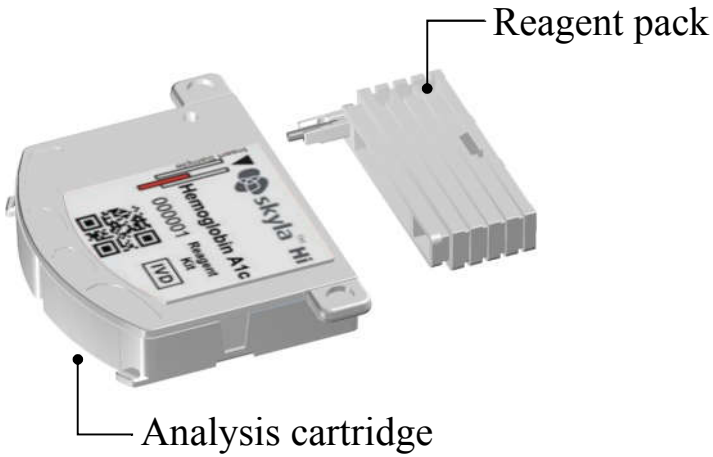
mean value for the past two months. Studies show that regular monitoring of glycated hemoglobin can be a reference for treating diabetes, while decreases in glycated hemoglobin values can serve as an indicator for metabolic control improvement.

3. Rationale

The product mainly uses "latex immuneagglutination as the methodology. Through a latex reagent, all hemoglobin can nonspecifically adhere to a latex sphere. When adding the HbA1c specific monoclonal antibody, the latex sphere will produce agglutination reaction, and the agglutination causes increased scattering of light, which is measured as an increase in absorbance at 650 nm. The HbA1c concentration is then quantified using a calibration curve of absorbance versus HbA1c concentration.

4. Test Components

The **skyla™** Hi Hemoglobin A1c Reagent kit consists of analysis cartridge and reagent pack (including of capillary tip for specimen collection).



Reagent and composition:

Location	Reagent	Composition
Reagent pack	Cell lysis buffer	Surfactant agent dissolved in a buffer.
	Latex solution	Latex particles dissolved in a buffer.
Analysis cartridge	Lyophilized bead with Antibodies	HbA1c specific mouse monoclonal antibodies and rabbit anti-mouse polyclonal antibodies dissolved in a buffer and then freeze-dried into spherical beads.

5. Storage and shelf life

- The kit under normal storage at 2~8°C in the refrigerator can be kept for up to one year. The expiry date of the reagent is printed on the outside of the sealed pouch of reagent kit.
- The test kit can be stored in unopened pouch at room temperature (15-25°C) for 12 weeks.

6. Specimen Collection and Preparation

The product is suitable for specimen, including fingertip whole blood and venous whole blood containing EDTA anticoagulant. The demand specimen volume for each test is about 0.8μL. The specimen is collected through the capillary tube on the reagent pack before test.

NOTE:

1. Once the reagent pack is filled with the blood sample, analysis must begin within five minutes.
2. Make sure that capillary is completely filled with sample.

3. Venous whole blood should be collected using a vacuum vessel containing EDTA coagulant. Can be stored refrigerated 2~8°C for one week

7. Testing Procedures

Material Preparation:

skyla™ Hi Hemoglobin A1c Reagent kit

Required materials not included in the kit:

skyla™ Hi Analyzer

Sample collection container with EDTA anticoagulant (for venous whole blood)

Finger lancets

Quality control solution

Test Conditions:

Test should be carrying out in an environment with temperatures of 10°C~32°C (50.0-89.6 °F). Each test will take about 6.5 minutes. During the test, chamber in the analyzer keeps the temperature at 37°C for stable assay.

Testing Steps:

1. Open the aluminum pouch and remove the analysis cartridge and reagent pack.
2. Use the reagent pack to collect samples.

Note: **Make sure that capillary is completely filled with sample as shown in figure (a) adequate. If the capillary is not completely filled with sample as shown in figure (b). Please repeat the collect samples**

procedure.

If the glass capillary exterior has excess blood buildup, use non-ciliated tissues to wipe away the excess blood outside the glass capillary.

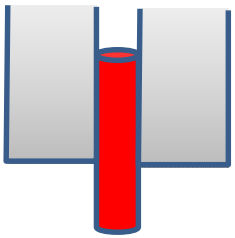


Fig. (a) adequate

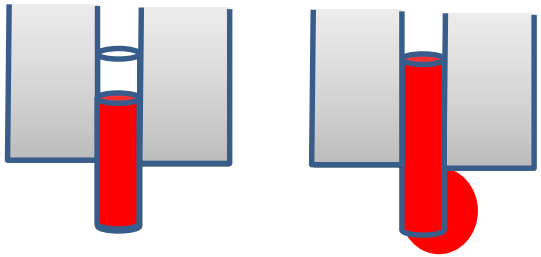


Fig. (b) inadequate

3. Insert the reagent pack in the analysis cartridge.
4. Affix the test cartridge into the analysis carrier.
5. Press the start button on the screen and place the carrier on the transmission tray of **skyla™ Hi Analyzer**. And then press "OK" button on the screen to initiate analysis.

Please refer to "skyla™ Hi Analyzer Operator's Manual" for addition information.

NOTE:

1. Once open the pouch, testing should be conducted within 20 minutes.
2. Be careful not to touch the optical window and bar-code on the analysis cartridge when performing the test.

8. Calibration

The analyzer automatically reads in the lot-specific calibration data from the barcode information printed on the analysis cartridge, eliminating the need for calibration by the user.

9. Quality Control

It's recommended to do the quality control testing routinely to ensure the reliability of measurement result.

The quality control testing with external control material is performed by following the regular testing steps shown above. The frequency and criteria of QC testing should be adapted to each site's individual requirements. The below shows the recommend timing of QC test that could be followed.

- At least every 30 days.
- Before a new batch of reagents is used for testing.
- When the analyzer is moved or the operating environment significantly changes.
- When an unexpected test results was obtained.

10. Result Reporting

The measured result is reported in both of NGSP (%) and IFCC (mmol/mol) units. The result will be directly display on the screen after each analysis, and also can be printed out through the external printer. Please refer to "skyla^{TM} Hi Analyzer Operator's Manual" for the detail description.

The reportable range of skyla^{TM} Hi Hemoglobin A1c Reagent kit is as follows: 4~15% (NGSP) or 20~140 mmol/mol (IFCC).

11. Expected value[1]

The American Diabetes Association (ADA) expected normal HbA1c range in adults is 4~6% (NGSP) or 20~42 mmol/mol (IFCC).

The ADA Clinical Practice Recommendation for diabetes specified a treatment goal of less than 7% and suggests additional action when HbA1c level is above 8%.

Each laboratory or test site should establish its own reference interval from its particular patient population.

12. Limitations/Interferences

Hemoglobin and Hematocrit:
The adapted concentration range of total hemoglobin of specimens is 7 to 20 g/dL (Hematocrit 20~60%). The test result may be affected if patient's hemoglobin value is outside the range.

Endogenous Interference:
The endogenous interference testing was performed using two HbA1c levels human specimen supplemented with known concentrations of the endogenous substances. No significant interference (<6%) was observed up to the following concentration.

Substance	Substance concentration with interference of less than ±6%
Conjugated bilirubin	20 mg/dL
Unconjugated bilirubin	20 mg/dL
Triglyceride	500 mg/dL
Urea	40 mg/dL

Exogenous Interference:
The exogenous interference testing was performed using two HbA1c levels human specimen supplemented with the maximum level of the exogenous substances that recommended in the CLSI EP7. No significant interference (<6%) was observed up to the following concentration.

Substance	Substance concentration with interference of less than ±6%

Acetaminophen	80 mg/dL
Aspirin	50 mg/dL
Ibuprofen	50 mg/dL
Ascorbic acid	5 mg/dL

Effect of labile glycated hemoglobin:
The effect of labile glycated hemoglobin was evaluated using two HbA1c levels human specimen that treated with high concentration of glucose (2000 mg/dL for 3.5 hr. at 37℃). No significant effect of labile glycated hemoglobin (up to 2000 mg/dL) was observed with this assay.

Effect of hemoglobin variant[8]:
Samples containing >10% HbF may result in lower than expected HbA1c results.

13. Performance Characteristics

Linearity:
The assay is linear between 4% and 15%.
Precision:
The precision of assay was evaluated with 5 levels of specimens by following the CLSI EP5 protocol. Tests are performed duplicates per run, 2 runs per day for a total of 20 days. Result for repeatability and reproducibility of assay is shown in the table below.

Specimens ID	Mean	Within-Run		Between-Run**		Between-Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
Y1	5.13	0.07	**1.4**	0.00*	**0.0***	0.07	**1.5**	0.10	**2.0**
Y2	9.27	0.17	**1.8**	0.00*	**0.0***	0.12	**1.3**	0.21	**2.3**
E9	5.19	0.11	**2.2**	0.05	**0.9**	0.08	**1.5**	0.15	**2.8**
E20	8.12	0.12	**1.5**	0.00*	**0.0***	0.08	**1.0**	0.15	**1.8**

Specimens ID	Mean	Within-Run		Between-Run**		Between-Day		Total	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV
7950	12.86	0.27	**2.1**	0.00*	**0.0***	0.24	**1.9**	0.36	**2.8**

**When the estimate of between-run SD is negative, it is set to 0 [CLSI EP-5: Evaluation of Precision Performance of Quantitative Measurements Methods, Repeatability Estimate.]*
***The Between-Run results are equal to Within-day [CLSI EP-5].*

Method comparison:

The HPLC based instrument was selected as comparative device in the study. Totally 42 human specimens between 4.5% and 11.9% were evaluated. Correlation between two methods can be determined through statistical analysis, and result is follows:

Regression line: $y = 1.012x - 0.13$

Correlation coefficient (R): 0.9912

14. Reference

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4. Quantitative measurement of HbA1c by an immunoturbidimetric assay compared to a standard HPLC method. American journal of clinical pathology. 1995, 104:89-95.
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Quantitative Measurement Methods; Approved Guideline - Second Edition. NCCLS document EP05-A2. 2004.

7. Clinical and Laboratory Standards Institute. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline - Second Edition. NCCLS document EP09-A2. 2002.
8. A Review of Variant Hemoglobins Interfering with Hemoglobin A1c Measurement. Journal of Diabetes Science and Technology, 2009, 3 (3):446-451.

Symbol Index			
REF	Catalogue number		Consult instruction for use
LOT	Batch code		Use by
	Manufacturer	EC REP	Authorised representative in the European Community
IVD	In Vitro diagnostic medical device	CE 0197	CE mark
	Temperature limitation		Caution
	Do not reuse		

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