InnovaStar®

oneHbA1c IS*

Order Information

Cat. No.	Kit size
1 3329 99 10 760	Σ 100 + 10 x 1800 µL Cleaner (Cat. No. 970112) + 1 x ParamCard (Cat. No. 970116)
970 100	InnovaStar® (instrument)
970 113	10 x 100 sample cups InnovaStar® 10/500
920 709	10 x 100 open-end capillaries 10 µL (Sodium-heparinized)
970 115	300 mL System solution InnovaStar®

Intended Use

Diagnostic reagent for quantitative in vitro determination of hemoglobin A1c in human sodium heparinized capillary whole blood on automated InnovaStar® for retrospective long-term monitoring of blood glucose concentration in individuals with diabetes mellitus and as an aid for diagnosis of diabetes mellitus. For professional use only.

Summary

Hemoglobin A1c (HbA1c) is a glycated hemoglobin which is formed by the non-enzymatic reaction of glucose with native hemoglobin. This process runs continuously throughout the circulatory life of the red cell (average life time 100 – 120 days). The rate of glycation is directly proportional to the concentration of glucose in the blood. The blood level of HbA1c represents the average blood glucose level over the preceding 6 to 8 weeks (due to the kinetics of erythrocyte turnover, this period is more affected by the blood glucose level than the preceding weeks). Therefore, HbA1c is suitable for retrospective long-term monitoring of blood glucose concentration in individuals with diabetes mellitus. Clinical studies have shown that lowering of HbA1c level can help to prevent or delay the incidence of late diabetic complications. Besides, HbA1c determination can be used as an aid for diagnosis of diabetes mellitus. As the amount of HbA1c also depends on the total quantity of hemoglobin, the reported HbA1c value is indicated as a percentage of the total hemoglobin concentration. [1-3]

Method

Particle enhanced immunoturbidimetric test

HbA1c is determined directly without measurement of total hemoglobin.

Total Hb and HbA1c in hemolyzed blood bind with the same affinity to particles in R1. The amount of binding is proportional to the relative concentration of both substances in the blood. Mouse anti-human HbA1c monoclonal antibody (R2) binds to particle bound HbA1c. Goat anti-mouse IgG polyclonal antibody (R3) interacts with the monoclonal mouse anti-human HbA1c antibody and agglutination takes place. The measured absorbance is proportional to the HbA1c bound to particles, which in turn is proportional to the percentage of HbA1c in the sample.

Standardization

The assay is standardized according to the approved IFCC reference method [4].

NGSP and IFCC values show a linear relationship and, therefore, can be calculated from each other using the following equation:

HbA1c *(IFCC[a])* = (HbA1c *(NGSP[b])* – 2.15)/0.0915

HbA1c *(NGSP[b])* = 0.0915 x HbA1c *(IFCC[a])* + 2.15

a: IFCC values in mmol/mol
b: NGSP values in %

IFCC: International Federation of Clinical Chemistry [4-6]
DCCT: Diabetes Control and Complications Trial [7]
NGSP: National Glycohemoglobin Standardization Program [8]

HbA1c and Average Glucose Concentrations [9]

Due to a linear correlation between hemoglobin A1c and average glucose concentrations, HbA1c values can be converted in estimated average glucose values by means of the following equations:

Standardization according to IFCC [9]:

Average glucose conc. [mg/dL] = 2.63 x HbA1c^a + 15.01

Average glucose conc. [mmol/L] = 0.146 x HbA1c^a + 0.829

a: HbA1c values in mmol/mol IFCC

Standardization according to NGSP:

Average glucose conc. [mg/dL] = 28.7 x HbA1c^b – 46.7
Average glucose conc. [mmol/L] = 1.59 x HbA1c^b – 2.59

b: HbA1c values in % NGSP

No significant differences in the regression equation were observed for variations in individuals tested, including sex, presence or absence of diabetes, type of diabetes, age, race, and ethnicity. Although this equation can be used for the majority of individuals, each laboratory has to reassure whether the regression equations mentioned are applicable for the patient group to be examined.

Reagents

Components and Concentrations

R1:	Buffer	20 mmol/L
	Latex	0.14%
R2:	Buffer	10 mmol/L
	Mouse anti-human HbA1c monoclonal antibody	5.5 mg/dL
R3:	Buffer	10 mmol/L
	Goat anti-mouse IgG polyclonal antibody	67 mg/dL

Storage and Stability

Reagents are stable up to the date of expiry indicated on the kit, if stored at 2 – 8°C. Do not freeze and protect from light. Do not use damaged or open reagent cartridges.

Warnings and Precautions

1. The reagents contain sodium azide (0.95 g/L) as preservative. Do not swallow! Avoid contact with skin and mucous membranes.
2. The reagent 2 and 3 contain material of biological origin. Handle the product as potentially infectious according to universal precautions and good clinical laboratory practice.
3. one HbA1c IS must not be used to diagnose diabetes during pregnancy [10].
4. Falsely low hemoglobin A1c values may occur in individuals suffering from diseases with shortened red cell survival times (hemolytic diseases) or significant recent blood loss [1].
5. Falsely high hemoglobin A1c values have been reported in iron deficiency anemia [3].
6. Heterophile antibodies in patient samples may cause falsified results.
7. In very rare cases, samples of patients with gammopathy might give falsified results [11].
8. In case of product malfunction or altered appearance that could affect the performance, contact the manufacturer.
9. Any serious incident related to the product must be reported to the manufacturer and the competent authority of the Member State where the user and/or patient is located.
10. Please refer to the safety data sheets (SDS) and take the necessary precautions for the use of laboratory reagents. For diagnostic purposes, the results should always be assessed with the patient's medical history, clinical examinations and other findings.

Waste Management

Refer to local legal requirements for chemical disposal regulations as stated in the relevant SDS to determine the safe disposal.

Warning: Handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Reagent Preparation

The reagents are ready to use. Bring reagent to room temperature. Make sure that the reagent is at the bottom of the cartridge.

Materials Required

General laboratory equipment

Specimen

Sodium heparinized capillary whole blood

Stability [12]:

Whole blood	1 week	at	2 – 8°C
Hemolysate	10 hours	at	15 – 25°C
Hemolysate	10 days	at	2 – 8°C

Discard contaminated specimens.

Sample Preparation

For sample preparation, sample cups InnovaStar® 10/500 (magenta cups) and open-end capillaries (10 µL/heparinized) are required. Take the patient sample with open-end capillary as described in the user manual. Put the filled capillary in the sample cup. Mix the sample and start the measurement directly.

Assay Procedure

Application is read by the ParamCard (see user manual InnovaStar®)

For each measurement of HbA1c, place a cup with cleaner (orange cup) in the last position of the slider.

Calibration

The calibration is stored on the ParamCard included in the reagent kit and is read after the receipt of the reagent (see user manual InnovaStar®). The calibration stability is 9 months. Fourteen days before the recalibration date, the instrument points to recalibration. This requires that a lot-specific code for a recalibration curve is entered into the instrument. For recalibration codes, refer to https://www.diasys-diagnostics.com/service-area/support/recalibration-of-innovastarr.

The procedure of entering the code is described in the user manual for InnovaStar®. The successful entry of the recalibration curve has to be verified by the measurement of controls. The calibration was performed with IFCC calibrators and is, therefore, traceable to the approved IFCC reference method.

Controls

Use a DiaSys TruLab HbA1c liquid control for internal quality control on every measuring day. An external quality control is recommended. Quality control must be performed after entering the recalibration code. Control intervals and limits have to be adapted to the individual requirements of each laboratory. Results must be within the defined ranges. Follow the relevant legal requirements and guidelines.

Each user should establish corrective action in case of deviation in control recovery.

	Cat. No.	Kit size
TruLab HbA1c liquid Level 1	5 9790 99 10 060	1 x 0.25 mL
TruLab HbA1c liquid Level 2	5 9800 99 10 060	1 x 0.25 mL

Performance Characteristics

Data evaluated on InnovaStar®

Measuring range up to 150 mmol/mol HbA1c according to IFCC (up to 16% according to DCCT/NGSP), depending on the concentration of the highest calibrator. The assay is applicable for total hemoglobin concentrations in blood from 6.6 to 26 g/dL.	
Limit of detection	30 mmol/mol HbA1c IFCC (4.9% HbA1c DCCT/NGSP)

Interferences

The study on interferences was conducted according to CLSI protocol EP7-A2.

IFCC

For each interfering substance, two samples with different HbA1c values have been tested; a low level sample within a HbA1c range of 20 – 40 mmol/mol and a high level sample within a HbA1c range of 60 – 100 mmol/mol.

DCCT/NGSP

For each interfering substance, two samples with different HbA1c values have been tested; a low level sample within a HbA1c range of 4.0 – 5.8% and a high level sample within a HbA1c range of 7.6 – 11.3%. The table below summarizes the results, which comply for all tested levels using IFCC as well as DCCT/NGSP standardization.

Interference by	**No interferences ≤ 7% DCCT/NGSP and ≤ 10% IFCC up to**
Ascorbic acid	60 mg/dL
Bilirubin (conjugated and unconjugated)	60 mg/dL
Glucose	1000 mg/dL
Hemoglobin (acetylated)	10 mmol/L
Hemoglobin (carbamylated)	10 mmol/L
Lipemia (triglycerides)	2000 mg/dL
N-acetylcysteine (NAC)	1500 mg/L
Rheumatoid factor	500 IU/mL
Urea	300 mg/dL
No interference is observed by Schiff base (labile intermediates) [12]. Alcoholism and ingestion of large doses of aspirin may lead to implausible results. For further information on interfering substances, refer to Young DS [13, 14].	

Hemoglobin variants [12]

The variants AS, AC, AD, AJ, AG, DD and elevated A2 showed no significant interferences.

The variants AE, SS, CC, SC, SE, EE, elevated F and elevated A2/F can lead to deviant HbA1c results.

Precision (Values according to DCCT/NGSP)			
Within run (n=20)	**Sample 1**	**Sample 2**	**Sample 3**
Mean [% DCCT/NGSP]	5.58	7.63	10.8
CV [%]	0.985	1.27	1.77
Day to day (n=20)	**Sample 1**	**Sample 2**	**Sample 3**
Mean [% DCCT/NGSP]	5.46	7.23	10.8
CV [%]	0.892	1.19	1.05
Total precision CLSI (n=80)	**Sample 1**	**Sample 2**	**Sample 3**
Mean [% DCCT/NGSP]	5.41	7.19	10.7
CV [%]	2.28	1.90	2.07

Method comparison (IFCC; n=100)	
Test x	Competitor HPLC HbA1c
Test y	DiaSys one HbA1c IS
Slope	1.08
Intercept	–0.435 %
Coefficient of correlation	0.997

Reference Range

Suggested target values for HbA1c [15]:

	mmol/mol IFCC	% NGSP
Non-diabetics	20 – 42	4 – 6
Target of therapy	< 53	< 7
Change of therapy	> 64	> 8

Each laboratory should check if the reference ranges are transferable to its own patient population and determine own reference ranges if necessary.

HbA1c cut point value for diagnosis of diabetes mellitus [3]:

According to a recommendation of the American Diabetes Association (ADA): ≥ 6.5% according to NGSP and 48 mmol/mol according to IFCC.

Patients with HbA1c values in the range of 5.7 – 6.4% HbA1c according to NGSP or 39 – 46 mmol/mol HbA1c according to IFCC may be at high risk of developing diabetes.

Literature

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Additions and/or changes in the document are highlighted in grey. For deletions, please refer to the customer information for the corresponding edition number of the package inserts.

IVD CE

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