HbA_1c DIRECT

En

REF No: 01R87-51 2286 Tests
REF No: 01R87-41 1143 Tests
REF No: 01R87-31 826 Tests
REF No: 01R87-21 571 Tests

FOR USE WITH
ARCHITECT

Diagnostic reagent for the determination of HbA1c concentration.
Liquid. Dual reagent. Store at +2/+8°C. For In Vitro Diagnostic use. **Do not freeze**.
The products with Ref Number mentioned above are produced for Abbott Architect c Systems.

Changes made in the instructions for use are marked as grey.

INTENDED USE

The Archem HbA1c test is used for the quantitative in vitro determination of HbA1c (hemoglobin fraction) in human whole blood samples by autoanalyzers in a clinical laboratory setting.

GENERAL INFORMATION

HbA1c forms irreversibly by glycosylation through enzymatic or non-enzymatic condensation of one or both of the N-terminal valines in the β-chains of the tetrameric hemoglobin A molecule. This can sometimes also occur by glycosylation of lysine residues in hemoglobin.[1]

The first form is the unstable schiff base (aldimine, pre-HbA1c) structure. The schiff base can dissociate or undergo Amadori rearrangement to form the HbA1c molecule, a stable ketoamine.[2]

The HbA1c test provides an index of average blood glucose levels over the last 2 to 4 months. Although red blood cells have a lifespan of about 120 days, HbA1c levels represent a "weighted" glucose level, with the youngest red blood cells contributing more than older ones. For glycemic control, it is recommended to measure and evaluate HbA1c levels every 3 to 6 months.[1]

The HbA1c test is used in both the diagnosis and follow-up of patients with Diabetes Mellitus (DM). In the follow-up of DM patients, an absolute difference in HbA1c test results between consecutive patient samples of %0.5 according to the National Glycohemoglobin Standardization Program (NGSP) or 5 mmol/mol according to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) is a clinically important change in glycemic control.[3]

The Diabetes Control and Complications Trial (DCCT) presented that lowering glucose levels in patients with type 1 diabetes slows and prevents the development of DM-related microvascular complications such as retinopathy, neuropathy and nephropathy. In the DCCT trials, a 50% to 75% reduction in complications was observed in the intensively treated group of patients whose HbA1c levels were reduced to %7.2 compared to those reduced to %9.0 in the conventionally treated group.[7] Similarly, a reduction in microvascular complications in type 2 DM patients has been reported in the United Kingdom Prospective Diabetes Study (UKPDS) and some other studies.[1,8]

According to the UKPDS study, reducing HbA1c from %7.9 (63 mmol/mol) to %7.0 (53 mmol/mol) in intensively treated patients decreases microvascular complications by 25% on average. In addition, in the UKPDS follow-up study, it was reported that major complications of DM also decreased due to this treatment approach.[1,2] For example, for every %1 reduction in HbA1c (e.g. from %8 to %7 [64 to 53 mmol/mol]), a 14% risk reduction in the incidence of myocardial infarction has been reported.[9] On the other hand, HbA1c levels in patients without DM are directly associated with cardiovascular disease. In the European Prospective Investigation on Cancer and Nutrition (EPIC-Norfolk) study, a %1 increase in HbA1c was associated with a 28% increased risk of death.[10]

There is no consensus on the frequency of optimal testing for both type 1 and type 2 DM patients. The ADA recommends routine monitoring of HbA1c at least every 6 months in patients who meet treatment goals (and have stable glycemic control).[11] In a study conducted on more than 79,000 patient were reported that the optimum test frequency should be every 3 months to maximize

decrease in HbA1c and less frequent testing has resulted in deterioration of control.[12]

HbA1c does not have sufficient specificity and sensitivity in the diagnosis of gestational diabetes mellitus (GDM).[2,13] Women with GDM should be screened for diabetes between 4-12 weeks after delivering by use OGTT criteria of non-pregnant. HbA1c is not recommended for antepartum treatment for hyperglycemia. If glucose values are normal, it is recommended that reassessment of glycemia should be done by use–glucose or HbA1c testing at least every 3 years.[2]

TEST PRINCIPLE

Immunoturbidimetric Measurement

More than 250 methods are used in the determination of glycehemoglobin (GHb). Most methods separate GHb from unglycated hemoglobin using techniques based on charge differences (ion exchange chromatography, HPLC, electrophoresis, and isoelectric focusing) or structural differences (affinity chromatography and immunoassay).[14] Some chemical analyzes (enzymatic, photometry, and spectrophotometry) and, more recently, capillary electrophoresis and enzymatic methods specifically measuring HbA1c have also become commercially available.[2]

Regardless of the method used, HbA1c results are expressed as a fraction of total hemoglobin. In this sense, the Archem HbA1c test states the percentage rate between total hemoglobin concentration (THb) and HbA1c concentration.

The antibody used in the Archem HbA1c test does not cross-react with labile HbA1c, making it specific for the ketoamine form of HbA1c. Stable HbA1c does not rise and fall in response to rapid changes in physiologic factors and therefore allows individuals to measure average blood glucose levels over several months.

This method uses the interaction of antigen and antibody to directly detect the HbA1c level in whole blood. THb and HbA1c molecules have a non-specific absorption rate against latex particles. When mouse anti-human HbA1c monoclonal antibody (R2) is added to the reaction medium, latex-HbA1c and mouse anti-human HbA1c antibody form a complex. When goat anti-mouse IgG polyclonal antibody is added to the medium, agglutination occurs. The amount of agglutination is proportional to the HbA1c absorbed onto the surface of the latex particles. The turbidity caused by agglutination is measured by absorbance reading at a wavelength of 660 nm (800 nm wavelength is used for dual wavelength preferences).

REAGENT COMPONENTS

Lyse Reagent	Reagent R1	Reagent R2:
Stabilizers Buffers, lysing agent, water	Latex: < 0,15 % Buffer Stabilizers.	Mouse anti-human HbA1c monoclonal antibody < 0.06 mg/mL, goat anti-mouse IgG polyclonal antibody < 0.09 mg/dL,Buffer, stabilizers.

REAGENT PREPARATION

R1 is ready to use. Use a calibrated and verified micropipette for preparation of the R2 reagent. With the help of a micropipette, take the following amount of R2b from the bottle and add it to the R2a vial. Cap the R2a vial and gently invert for 30-40 seconds to ensure homogeneous mixing of the R2b. Use only its cover to avoid contamination. If air bubbles are present in the reagent vial, remove them with a new applicator stick. After preparing the reagent, leave it for 30 minutes at +2/+8°C. After waiting 30 minutes, you can use the reagent.

REF Number	R2a	Amount of R2b to be used
01R87-51	19 mL	1 mL (1000 µL)
01R87-41	14,25 mL	0,75 mL(750 µL)
01R87-31	7,55 mL	0,45 mL(450 µL)
01R87-21	14,55 mL	0,75 mL(750 µL)

REAGENT STABILITY AND STORAGE

The reagents are stable until the expiration date stated on the label as long as they are kept at +2/+8°C.

Once opened vials are stable for 30 days at +2/+8°C in optimum conditions. On board stability is strongly related to auto analyzers' cooling specification and carry-over values.

Reagent stability and storage data have been verified by using Clinical and Laboratory Standards Institute (CLSI) EP25-A protocol.[15]

SAMPLE REQUIREMENTS

Human anticoagulated venous whole blood is the recommended specimen type for this test. Recommended anticoagulants are dipotassium ethylenediaminetetetraacetate (K2-EDTA) or tripotassium EDTA (K3-EDTA). Storage conditions for samples not to be processed immediately:

3 days at +15/+25°C
7 days at +2/+8°C
6 months at -20°C

Freeze and thaw only for one time.

To mobilize erythrocytes before starting the test, gently swirl and mix whole blood samples until homogenized.

TEST PROCEDURE

Hemolysate Preparation,

1) Whole blood samples are brought to room temperature.
2) The blood samples are mixed so that the erythrocytes are homogeneously mixed.
3) Using a calibrated pipette, transfer 1000 µL of Lyse solution to the specimen container.
4) 40 µL of homogenized blood sample is transferred into the sample container with Lyse added.
5) The hemolysate is mixed thoroughly and incubated for 5 minutes at room temperature.
6) The hemolysate is ready to use for HbA1c.

CALIBRATION AND QUALITY CONTROL

Calibration: The assay requires the use of an HbA1c Direct Calibrator 4-Level. We recommend:

HbA1c Direct Calibrator 4-Level
Ref. No: 01R97-01

Calibration stability depends on the application characteristics and cooling capacity of the autoanalyzer used. Calibration stability is 30 days.

The closed calibrator vials are stable at +2/+8°C until the expiry date. HbA1c Calibrator Set is supplied in lyophilized form.

The lyophilized content should be reconstituted with the amount of deionized water indicated on the label according to the instructions and used after 30-minute waiting. It is recommended to store the diluted calibrators at +2/+8˚C in sample cups compatible with the autoanalyzer, tightly capped. Calibrators stored at +2/+8˚C in this way are stable for 30 days.

Control: Commercially available control material with established values determined by this method can be used. We recommend:

HbA1c Direct Control Set (Low/High)
Ref. No: 01R96-01

Closed control vials are stable at +2/+8°C until their expiry date. HbA1c Control Kit is supplied in lyophilized form. The lyophilized content should be reconstituted with the amount of deionized water indicated on the label according to the instructions and used after 30-minute waiting. It is recommended to store the diluted controls at +2/+8˚C in sample containers compatible with the autoanalyzer, tightly capped. Controls stored at +2/+8˚C in this way are stable for 30 days.

2 levels HbA1c controls must be run once in every 24 hours. Each laboratory should determine its own quality control scheme and procedures. If quality control results are not within acceptable limits, calibration is required.

HBA1C TEST RESULT REPORTING

SI Units (IFCC):

The IFCC method reports HbA1c in mmol/mol (HbA1c/total Hb)[16] and is automatically calculated by the system using the following formula:[17]

mmol/mol HbA1c IFCC:
HbA1c (mmol/mol) = (HbA1c/THb) × 1000

Conventional Units (NGSP):

According to the NGSP method, HbA1c is reported as a percentage of total hemoglobin in the NGSP system. These values, equivalent to those reported by DCCT and UKPDS, represent the most widely used reporting system in patient care and published literature.

Comparison between the IFCC and NGSP networks has produced a master equation that allows conversion between the two reference systems.[18] For example, an HbA1c result of %7.0 (in NGSP/DCCT/UKPDS units) is equivalent to 53 mmol/mol (in IFCC units). Unit conversion calculators are freely available on various websites such as **http://www.ngsp.org/convert1.asp**.[2] The unit conversion calculation is based on the formula given below:

NGSP%= [0.09148 x (IFCC)] + 2.152

Many journals now require HbA1c to be reported in both NGSP/DCCT and SI units.[16]

The Relationship Between HbA1c and Glucose:

In a prospective study involving a large number of countries, the relationship between HbA1c concentrations and long-term glucose values was evaluated. As a result of the study, it was determined that there is a linear correlation obtained from HbA1c measurement that allows the calculation of estimated average glucose (eAG).[19]

The regression equations are as follows:

eAG mg/dL= 28.7 × HbA1c - 46.7 and
eAG mmol/L= 1.59 × HbA1c – 2.59

For example, an HbA1c value of %7.0 (53 mmol/mol) implies an eAG of 140 mg/dL. Some clinicians and many diabetes educators believe that eAG will facilitate communication with patients.[20] The ADA and AACC recommend that laboratories report both HbA1c and eAG. However, the concept of expressing HbA1c in terms of mean glucose is not universally accepted.[21,22]

REFERENCE INTERVAL / MEDICAL DECISION LEVELS

HbA1c values are expressed as a percentage of total blood hemoglobin. In the past, it was measured as one of the three main types of HbA1c, namely HbA1, HbA1c or total GHb. Today, many countries, including the United States, Canada, Australia, New Zealand and the United Kingdom, report all results as HbA1c.

Today, blood glucose concentrations as well as HbA1c values are widely used to diagnose DM and identify people at high risk of DM. The target values for DM and high DM risk determined by the ADA based on HbA1c values are as follows:[6]

Rec.* Diagnosis	HbA1c (%)	HbA1c (mmol/mol)
Diabetic	≥ 6,5	≥ 48
Prediabetes	5,7 – 6,4	39 – 47
Normal	< 5,7	< 39

** Rec.: Recommended*

NOTE: % values are given in NGSP, and mole values are given in IFCC units.

In 2009, the recommendation[4,5] by the International Committee of Experts (ICP) to admit the HbA1c clinical decision point of %6.5 (48 mmol/mol) as the diagnostic criterion for type 2 DM was adopted by many leading clinical organizations such as the American Diabetes Association (ADA)[6] the World Health Organization (WHO), and the European Association for the Study of Diabetes (EASD) and has been widely used as the diagnostic criterion for type 2 DM.[2,4]
However, target values established by the DCCT and UKPDS and recommended by ADA and other organizations are used to assess metabolic control in DM patients, not reference values.

There is no specific HbA1c value that demonstrates complete elimination of the risk of developing DM complications. ADA states that, in general, the goal of treatment should be to maintain HbA1c below %7.0 (53 mmol/mol), while other organizations recommend an HbA1c target below %6.5 (48 mmol/mol).[2,11]

In pregnant women with pre-existing DM, HbA1c should be aimed to be below %6.5 to protect the fetus from congenital malformations and the baby and mother from complications (These target values are only valid if the test method is certified by NGSP according to the DCCT reference).[2]

The effects of age on the reference interval are controversial.[28] Some studies report an age-related increase (≈0.1% per decade after age 30), while other studies show no increase in non-diabetic individuals.[24,25]

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary, determine its own reference range.

The reference interval has been verified using CLSI EP28-A3c protocol.[26]

LIMITATIONS

- The linearity of the measurement method is up to %15.5 HbA1c. Samples with values below %15.5 should not be reconstituted and/or retested.
- The values of DM patients with poor glycemic control, may increase up to twice or more the upper limit of the reference interval but rarely exceed %15.0 HbA1c. Values higher than %15.0 (140 mmol/mol) or lower than %4.0 (20 mmol/mol) require additional investigations to determine the possible presence of variant hemoglobin.[27] In this case, HbA1c should be repeated, if possible, using a method with a different analytical principle than the initial test.[2]
- The interpretation of HbA1c depends on red blood cells with normal lifespan. Patients with hemolytic disease or other conditions that shorten red blood cell lifespan may have significant reductions in HbA1c test results.[27]
- Individuals with recent significant blood loss may have erroneously low values due to a higher fraction of young erythrocytes.[2]
- Race affects HbA1c concentration. Published evidence shows that HbA1c concentrations are higher in individuals of black, Asian and Latin American descent than in whites.
- Inconsistencies have been observed with high doses of acetylsalicylic acid and narcotic drugs and in the results of some intoxicated patients.
- Whole blood samples collected in anticoagulated vacutainers, except those containing EDTA, should not be used.
- High levels of HbF may lead to inadequate assessment of HbA1c.

PERFORMANCE CHARACTERISTICS

Measuring Interval

According to CLSI EP34-ED1:2018, “Measuring Interval” refers to the interval where the analyte concentration is measured with intended accuracy in terms of medical and laboratory requirements without dilution, concentrating or any kind of pre-treatment that is between the analyte’s lower limit of quantitation (LLoQ) and upper limit of quantitation (ULoQ).[28]

The measuring interval of the HbA1c test: %4.0 - %15.5 (20-146 mmol/mol).

Detection Capability

Limit of Quantitation (LoQ): %4.0

Note: LoQ values are based on Coefficient of Variation Percentage (CV) ≤ 20%.

LoQ value has been verified by using CLSI EP17-A2:2012 protocol.[29]

Linearity

This method shows measurement linearity in the activities up to %15.5. For samples with results above %15.5, the manual dilution procedure described below should be applied.

Manuel Dilution Procedure

Recommended Dilution: 1:2

1. Add 250 µL of whole blood from the sample to be measured to 250 µL of a known low HbA1c sample (i.e., <%6.0 HbA1c), and thoroughly mix before testing.

Note: Manuel Dilution Procedure is only be applied if both of the patient sample and the lower HbA1c samples Hb concentrations are between 7 – 20 g/dL.

2. The result must be higher than %4.0 HbA1c before the dilution calculation is going to be applied.

3. Calculate the sample value using the equation bellow;

Sample value (%): Concentration Observed x 2 – Lower Sample Concentration

Linearity studies data have been verified by using CLSI EP06-A:2003 protocol.[30]

Precision

Running system has been developed according to 20x2x2 "The Single Site" protocol. Repeatability and Within-Laboratory Precision/Within-Device values have been obtained according to the running results.

According to the protocol in use, 2 separate runs per day have been made for 20 days (no obligation for being consecutive days).

This protocol has been applied to each low and high samples separately and 80 results have been obtained for each one. Statistically, the results have been obtained using 2-factor Nested-ANOVA model.[31]

Repeatability (Within Run) and Repeatability (Day to Day) SD and CV% values of HbA1c have been given in the table 1 and 2 respectively.

Table 1. HbA1c Repeatability (Within Run) results obtained from samples in two different concentrations

Mean Concentration (%)	CV%	n
5.57	0.60	80
11.82	1.00	80

*SD: Standard Deviation

Note: This working system has been named "Within-Run Precision" in the previous CLSI - EP05-A2 manual.[32]

Table 2. HbA1c Repeatability (Day to Day) results obtained from samples in two different concentrations

Mean Concentration (%)	CV%	n
5.57	1.00	80
11.82	1.90	80

Note: This working system has been named "Total Precision" in the previous CLSI - EP05-A2 manual.[32]

Interference

Endogenous interferant and analyte concentrations that have been used in the HbA1c scanning tests has been determined according to "CLSI EP37-ED1:2018" and "CLSI EP07-ED3:2018" manuals.[33,34]

The total acceptable error rate, which is going to be used to detect whether the observed differential value obtained from HbA1c interference scanning test is appropriate, is determined as ±10%.[35]

In HbA1c test results, no significant interaction has been observed in the determined endogenous interferant and analyte concentrations or between interferants and analyte.

Interferent and Concentration	HbA1c Target (%)	N	% Observed Recovery
Bilirubin 58,5 mg/dL	5,60	5	%99
	8,70		%96
Triglyceride 5040 mg/dL	6,80	5	%100
	9,70		%99

It should be noted that endogenous interferants, as well as various medicines and metabolites, anticoagulants (e.g. Heparin, EDTA, citrate, oxalate) and preservatives (e.g. sodium floride, iodoacetate, hydrochloride acide) such as additives, materials that may contact with samples during collection and processing (serum separator devices, sample collection containers and contents, catheters, catheter wash solutions, skin disinfectants, hand cleaners and lotions, glass washing detergents, powder gloves), dietary substances known to affect some specific tests (caffeine, beta-carotene, poppy seeds, etc.), or some substances present in a sample that cause foreign proteins (heterophilic antibodies, etc.), autoimmune response (autoantibodies, etc.), or due to malignancy (for example, interference by paraproteins with phosphate testing and indirect ion selective electrode methods) may show some negative effects that will cause various attempts and some misjudgements.[34]

Interferences due to drug treatments or endogenous substances may affect the results.

These performance characteristics have been obtained using an autoanalyzer. Results may vary slightly when using different equipment or manual procedures.

WARNINGS AND PRECAUTIONS

IVD: For in Vitro Diagnostic use only.
Do not use expired reagents.
Reagents with two different lot numbers should not be interchanged.
For professional use.
Follow Good Laboratory Practice (GLP) guidelines.

CAUTION: Human source samples are processed with this product. All human source samples must be treated as potentially infectious materials and must be handled in accordance with OSHA standards.

Danger

EUH032	:Releases a very toxic gas if contacts with acid.
H317	:May cause allergic skin reaction.

Precaution

P280	:Use protective gloves / clothes / glasses / mask.
P264	:Wash your hands properly after using.
P272	:Contaminated work clothes should not be allowed to be used outside of the workplace.

Intervention

P302+P352	:Wash with plenty of water and soap if it contacts with skin.
P333+P313	:Seek medical help if it irritates your skin or develops rash.
P362+P364	:Remove contaminated clothes and wash properly before using.

Disposal

P501	:Dispose the vials and contents according to the local regulations.

REFERENCES

1. McPherson, R. A., Pincus, M. R., (2017) Henry's Clinical Diagnosis and Management by Laboratory Methods (23rd ed.), p.252, Elsevier, St. Louis, Missouri 63043.
2. Rifai, N., Chiu, R. W., & Young, I., et al., (2023) Tietz Textbook of Laboratory Medicine (7th ed.), Chapter 47: Diabetes Mellitus, p.502-43.e12, Elsevier, St. Louis, Missouri 63043
3. Rifai, N., Chiu, R. W., & Young, I., et al., (2023) Tietz Textbook of Laboratory Medicine (7th ed.), Chapter 10: Evidence-Based Laboratory Medicine, p.194-e21, Elsevier, St. Louis, Missouri 63043
4. The International Expert Committee. International expert committee report on the role of the A1c assay in the diagnosis of diabetes. Diabetes Care 2009;32:1327–34.
5. Sacks DB. The diagnosis of diabetes is changing: how implementation of hemoglobin A1c will impact clinical laboratories. Clin Chem 2009;55:1612–4.
6. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010;33(Suppl 1):S62–9.
7. Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin dependent diabetes mellitus, *N Engl J Med* 329:977–986, 1993
8. Ohkubo Y, Kishikawa H, Araki E, et al: Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with noninsulin-dependent diabetes mellitus: A randomized prospective 6-year study, *Diabetes Res Clin Pract* 28:103–117, 1995.
9. U.K. Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352:837–53.
10. Khaw KT, Wareham N, Luben R, et al. Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of European prospective investigation of cancer and nutrition (EPICNorfolk). BMJ 2001;322:15–8.
11. American Diabetes Association. Standards of medical care in diabetes —2009. Diabetes Care 2009;32(Suppl 1):S13–61.
12. Driskell OJ, Holland D, Waldron JL, et al. Reduced testing frequency for glycated hemoglobin, HbA1c, is associated with deteriorating diabetes control. Diabetes Care 2014;37:2731–7.
13. Wexler DJ, Powe CE, Barbour LA, et al. Research gaps in gestational diabetes mellitus: executive summary of a National Institute of Diabetes and Digestive and Kidney Diseases Workshop. Obstet Gynecol 2018;132:496–505.
14. Goldstein DE, Little RR, Wiedmeyer H-M, England JD, Rohlfing CG. Glycated haemoglobin estimation in the 1990s: a review of assay methods and clinical interpretation. In: Marshall SM, Home PD, editors. The diabetes annual. New York: Elsevier Science B. V.; 1994. p. 193–212.
15. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline. CLSI Document EP25-A. Wayne, PA: CLSI; 2009.
16. Sacks DB. Measurement of hemoglobin A(1c): a new twist on the path to harmony. Diabetes Care 2012;35:2674–80.
17. Geistanger A, Arends S, Berding C, et al. Statistical methods for monitoring the relationship between the IFCC reference measurement procedure for hemoglobin A1c and the designated comparison

methods in the United States, Japan, and Sweden. *Clin Chem* 2008; 54(8): 1379 – 1385.
18. Hoelzel W, Weykamp C, Jeppsson JO, et al. IFCC reference system for measurement of hemoglobin A1c in human blood and the national standardization schemes in the United States, Japan, and Sweden: a method-comparison study. Clin Chem 2004;50:166–74.
19. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ. Translating the hemoglobin A1c assay into estimated average glucose values. Diabetes Care 2008;31:1473–8.
20. Sacks DB. Translating hemoglobin A1c into average blood glucose: Implications for clinical chemistry. Clin Chem 2008;54:1756–58.
21. Kilpatrick ES. Haemoglobin A1c in the diagnosis and monitoring of diabetes mellitus. J Clin Pathol 2008;61:977–82.
22. Little RR, Sacks DB. HbA1c: how do we measure it and what does it mean? Curr Opin Endocrinol Diabetes Obes 2009;16:113–8.
23. Sacks DB, Arnold M, Bakris GL, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2011;57:e1–47.
24. Pani LN, Korenda L, Meigs JB, et al. Effect of aging on A1C levels in individuals without diabetes: evidence from the Framingham Offspring Study and the National Health and Nutrition Examination Survey 2001-2004. Diabetes Care 2008;31:1991–6.
25. Wiener K, Roberts NB. Age does not influence levels of HbA1c in normal subject. QJ Med 1999;92:169–73.Pozzi C, Bolasco PG, Fogazzi GB, et al. Corticosteroids in IgA nephropathy: a randomised controlled trial. Lancet 1999; 353:883–7.
26. Clinical and Laboratory Standards Institute (CLSI). Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition. CLSI Document EP28-A3c. Wayne, PA: CLSI; 2010.
27. Bry L, Chen PC, Sacks DB. Effects of hemoglobin variants and chemically modified derivatives on assays for glycohemoglobin [Review]. Clin Chem 2001;47:153–63.
28. Clinical and Laboratory Standards Institute (CLSI). Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking - First Edition. CLSI Document EP34. Wayne, PA: CLSI; 2018.
29. CLSI EP17-A protocol. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition. CLSI Document EP17-A2. Wayne, PA: CLSI; 2012.
30. Clinical and Laboratory Standards Institute (CLSI). Evaluation of the Lineari ty of Quantitative Measurement Procedures: A Statistical Approach - 1st Edition. CLSI Document EP06-A. Wayne, PA: CLSI; 2003.
31. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition. CLSI Document EP05-A3. Wayne, PA: CLSI; 2014.
32. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – 2nd Edition. CLSI Document EP05-A2. Wayne, PA: CLSI; 2004.
33. Clinical and Laboratory Standards Institute (CLSI). Supplemental Tables for Interference Testing in Clinical Chemistry - First Edition. CLSI Document EP37. Wayne, PA: CLSI; 2018.
34. Clinical and Laboratory Standards Institute (CLSI). Interference Testing in Clinical Chemistry - Third Edition. CLSI Document EP07. Wayne, PA: CLSI; 2018.
35. CLIA proficiency testing criteria for acceptable analytical performance, as printed in the Federal Register July 11, 2022;87(131:41194-242.

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CE

SYMBOLS

IVD	In Vitro Diagnostic Medical Device
LOT	Lot Number
R1	Reagent 1
R2	Reagent 2
GTIN	Global Trade Item Number
REF	Reference Number
GLP	Good Laboratory Practices
FOR USE WITH	Identifies Products to Be Used Together
PRODUCT OF TURKEY	Product of Turkey
	Manufacturer
	Expiration Date
	Temperature Limits
	Consult Instructions for Use
	Caution
	Number of Tests