SIEMENS Healthineers

Enzymatic Hemoglobin A1c (A1c_E)

Current Revision and Date[a]	Rev 03, 2021-10	
Product Name	Atellica CH Enzymatic Hemoglobin A1c (A1c_E)	REF 11097536 (600 tests)
Abbreviated Product Name	Atellica CH A1c_E	
Test Name/ID	A1c_E	
Systems	Atellica CH Analyzer	
Materials Required but Not Provided	Atellica CH A1c_E CAL	REF 11099338
Specimen Types	Human anticoagulated venous whole blood	
Sample Volume	4.5 µL	
Measuring Interval	3.80–14.00 %HbA1c (18.03–129.50 mmol/mol HbA1c)	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

CE

Intended Use

The Atellica® CH Enzymatic Hemoglobin A1c (A1c_E) assay is an *in vitro* diagnostic assay for the quantitative determination of mmol/mol HbA1c (IFCC) and %HbA1c (DCCT/NGSP) in human anticoagulated venous whole blood for use on the Atellica® CH Analyzer. Measurement of hemoglobin A1c is used as an aid in the diagnosis and monitoring of long-term blood glucose control in patients with diabetes mellitus, and as an aid in the identification of patients at risk for developing diabetes mellitus.

Summary and Explanation

HbA1c is formed by the non-enzymatic glycation of the N-terminus of the β-chain of hemoglobin A. The HbA1c level reflects the mean glucose concentration over the previous period (approximately 8–12 weeks, depending on the individual) and provides better indication of long-term glycemic control than blood and urinary glucose determinations.[1] Studies have shown that long term control of HbA1c levels can decrease the risk for development and progression of chronic complications caused by diabetes.[2,3]

Principles of the Procedure

The Atellica CH A1c_E assay consists of two separate measurements: glycated hemoglobin (A1c_E) and total hemoglobin (tHb_E). The two measurements are used to determine the %HbA1c (NGSP units) or the hemoglobin A1c_E/tHb_E ratio in mmol/mol (IFCC units). The individual concentration values of A1c_E and tHb_E generated by this assay are used only for calculating the %HbA1c or A1c_E/tHb_E ratio, and must not be used individually for diagnostic purposes.

The anticoagulated whole blood specimen is lysed on the system using the Atellica CH A1c_E pretreatment solution to obtain hemolysate for the Atellica CH A1c_E assay.

The Atellica CH A1c_E assay is an enzymatic method that specifically measures N-terminal fructosyl dipeptides on the beta-chain of HbA1c. In the pretreatment step, the erythrocytes are lysed and the hemoglobin is oxidized to methemoglobin by reaction with sodium nitrite. In the first step of the reaction (the Atellica CH A1c_E reagent 1 (R1) + sample), the N-terminal fructosyl dipeptide fragment is cleaved from the hemoglobin beta chain with a protease. Concurrently, methemoglobin is converted into stable azide-methemoglobin in the presence of sodium azide and the total hemoglobin concentration is determined by measuring the absorbance at 478/694 nm. In the second step of the reaction, fructosyl peptide oxidase (FPOX) is added to react with the fructosyl dipeptide to generate hydrogen peroxide. The hydrogen peroxide reacts with the chromogen in the presence of peroxidase to develop a color that is measured at 658/805 nm.

The Atellica CH A1c_E assay incorporates a turbidity normalization mechanism (cHb_E) that is measured at 805 nm to effectively remove any sample turbidity which could impact the tHb_E measurement.

Reagents

Material Description	Storage	Stability[a]
Atellica CH A1c_E	Unopened at 2–8°C	Until expiration date on product
Pack 1 (P1)	Onboard per well	63 days
Well 1 (W1) Reagent 1 (R1) 16.5 mL 10-Carboxymethylaminocarbonyl-3,7-bis (dimethylamino)-phenothiazine sodium salt (0.000817%); sodium azide (< 0.1%); protease (Bacterial, < 10 mU/L); ProClin 300		
Well 2 (W2) Reagent 1 (R1) 16.5 mL 10-Carboxymethylaminocarbonyl-3,7-bis (dimethylamino)-phenothiazine sodium salt (0.000817%); sodium azide (< 0.1%); protease (Bacterial, < 10 mU/L); ProClin 300		
Pack 2 (P2)		
Well 1 (W1) Reagent 2 (R2) 8.0 mL Peroxidase (Horseradish, 50–150 kU/L); fructosyl peptide oxidase (E. coli, recombinant, 3–9 kU/L); ofloxacin		
Well 2 (W2) Reagent 2 (R2) 8.0 mL Peroxidase (Horseradish, 50–150 kU/L); fructosyl peptide oxidase (E. coli, recombinant, 3–9 kU/L); ofloxacin		
Vial 1 (A1c_E PRE)	Unopened at 2–8°C	Until expiration date on product
35.65 mL Sodium nitrite (> 0.05–< 0.3%); ProClin 300; maleic acid (< 1%)	Onboard per vial	63 days

[a] Refer to *Storage and Stability*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

Safety data sheets (SDS) available on siemens.com/healthineers.

H317 **P280, P272, P302+352, P333+P313, P363, P501**	**Warning!** May cause an allergic skin reaction. Wear protective gloves/protective clothing/eye protection/face protection. Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains:** 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (R1 and A1c_E PRE); Maleic acid (A1c_E PRE)

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Storage and Stability

Protect the product from heat and light sources. Unopened reagents are stable until the expiration date on the product when stored at 2–8°C. Do not freeze reagents.

For information about storage and stability of materials in the Cal-QC tube storage area, refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability."

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 63 days. Discard reagents at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

Specimen Collection and Handling

Human anticoagulated venous whole blood is the recommended sample type for this assay.

Recommended anticoagulants are dipotassium ethylenediaminetetraacetate (K_2-EDTA), lithium heparin, sodium fluoride/disodium EDTA, or tripotassium EDTA (K_3-EDTA).

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[4]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[5]
- Follow the instructions provided with your specimen collection device for use and processing.[6]
- Keep tubes capped at all times.[7]

Storing the Specimen

Specimens may be stored for up to 48 hours at room temperature,[8] for up to 7 days at 2–8°C,[8] or stored frozen for up to 21 months (with one freeze-thaw) at -70°C.[8]

Refer to *Preparing the Samples* for more information.

The handling and storage information provided here is based on data or references maintained by the manufacturer. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Preparing the Samples

This assay requires 4.5 µL of sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

Note Do not use specimens with apparent contamination.

Before placing samples on the system:

- Ensure that samples are free of bubbles or foam.
- Ensure that samples are free of fibrin or other particulate matter.
- Thaw frozen samples at room temperature and mix thoroughly prior to use.
- Do not refreeze thawed samples.
- Thoroughly mix all blood samples immediately before testing to ensure valid results.

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11097536	**Pack 1 (P1)** Well 1 (W1) 16.5 mL of Atellica CH A1c_E Reagent 1 Well 2 (W2) 16.5 mL of Atellica CH A1c_E Reagent 1 **Pack 2 (P2)** Well 1 (W1) 8.0 mL of Atellica CH A1c_E Reagent 2 Well 2 (W2) 8.0 mL of Atellica CH A1c_E Reagent 2 **Vial 1 (A1c_E PRE)** 2 x 35.65 mL of Atellica CH A1c_E PRE	2 x 300

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

REF	Description	
	Atellica CH Analyzer[a, b]	
11099338	Atellica CH A1c_E CAL (calibrator)	1 x 5.0 mL calibrator level 1 CAL 1 2 x 1.0 mL calibrator level 2 CAL 2 2 x 1.0 mL calibrator level 3 CAL 3 Calibrator lot-specific value sheet CAL LOT VAL
	Commercially available quality control materials	

[a] Additional system fluids are required to operate the system: Atellica CH Diluent, Atellica CH Wash, Atellica CH Conditioner, Atellica CH Cleaner, Atellica CH Reagent Probe Cleaner 1, Atellica CH Reagent Probe Cleaner 2, Atellica CH Reagent Probe Cleaner 4, Atellica CH Lamp Coolant, and Atellica CH Water Bath Additive. For system fluid instructions for use, refer to the Document Library.

[b] For system fluid instructions for use, refer to the Document Library.

Assay Procedure

The system automatically performs the following steps:

1. For whole blood, dispenses 4.5 µL of primary sample and 100 µL of Atellica CH A1c_E PRE into a dilution cuvette.
2. Dispenses 80 µL of Reagent 1 into a reaction cuvette.
3. Dispenses 8.3 µL of pre-diluted sample into a reaction cuvette.
4. Mixes and incubates the mixture at 37°C.
5. Measures the absorbance for tHb.
6. Dispenses 27 µL of Reagent 2 into a reaction cuvette.
7. Mixes and incubates the mixture at 37°C.
8. Measures the absorbance for A1c.
9. Reports results.

Test Duration: 10 minutes

Preparing the Reagents

All reagents are liquid and ready to use.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. For information about loading reagent packs, refer to the online help.

Performing Calibration

For calibration of the Atellica CH A1c_E assay, use Atellica CH A1c_E CAL.

Use the calibrators in accordance with the calibrator instructions for use.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service, if indicated by quality control results.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	180
Pack Calibration	63
Reagent Onboard Stability	63

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Performing Quality Control

For quality control of the Atellica CH A1c_E assay, use at least two levels (low and high) of the appropriate quality control material of known analyte concentration. Use the quality control material in accordance with the quality control instructions for use.

For the assigned values, refer to the lot-specific value sheet provided. A satisfactory level of performance is achieved when the analyte values obtained are within the expected control range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the online help.

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The National Glycohemoglobin Standardization Program (NGSP) and the International Federation of Clinical Chemistry (IFCC) formed a working group to develop better primary reference methods. The relationship between HbA1c results from the NGSP network and the IFCC network was evaluated and a master equation was developed.[8,9]

Results generated on the Atellica CH Analyzer are in either NGSP equivalent units (%HbA1c) or IFCC equivalent units (mmol/mol).

Conversion formula: %NGSP = (0.09148 x IFCC) + 2.152

The system automatically calculates, and reports results based on the absorbance measurements of the test sample during the test, and of the calibrator(s) from calibration.

The system calculates A1c_E and tHb_E results in µmol/L (SI units). To convert the A1c_E or the tHb_E results to g/dL (conventional units), use the following equation:

Conversion factor: µmol/L x 0.09356 = g/dL

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

Interpretation of Results

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Limitations

WARNING
The Atellica CH A1c_E assay has significant interference with fetal hemoglobin (HbF). Samples containing HbF may produce a negative bias (lower than actual results) with the Atellica CH A1c_E assay. Hemoglobin A1c results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin. For additional information on the interference of the HbF variant, refer to *Hemoglobin Variants*.

The Atellica CH A1c_E assay is limited to the detection of HbA1c in human anticoagulated venous whole blood.

Patients with hemoglobin concentrations outside of the acceptable range for the Atellica CH A1c_E assay should be assayed by a test employing a different assay principle.

The Atellica CH A1c_E assay should not be used to diagnose diabetes during pregnancy. Hemoglobin A1c reflects the average blood glucose levels over the preceding 8–12 weeks (the average life span of a red blood cell) and therefore may be falsely low during pregnancy or any other condition associated with recent onset of hyperglycemia and/or decreased red blood cell survival.

The Atellica CH A1c_E assay should not be used to diagnose or monitor diabetes in patients with the following conditions: hemoglobinopathies except as demonstrated to produce acceptable performance (such as sickle cell trait), abnormal red blood cell turnover (such as anemias from hemolysis and iron deficiency), malignancies, and severe chronic hepatic and renal disease.

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 concentrations and/or the typical clinical symptoms.

Any cause of shortened red blood cell survival (for example, hemolytic anemia or other hemolytic diseases, pregnancy, or recent significant blood loss) will reduce exposure of red blood cells to glucose with a consequent decrease in HbA1c values. HbA1c results are not reliable in patients with chronic blood loss and consequent variable erythrocyte life span.

Fetal hemoglobin (HbF) consists of 2 alpha and 2 gamma chains that are not recognized by the FPOX enzyme which measures N-terminal fructosyl dipeptides on the beta-chain (refer to *Principles of the Procedure*). Samples that contain high amounts of HbF, usually found in some people with thalassemia, in infants, and in some pregnant women, may yield a lower than expected HbA1c result with this assay.

This test should not replace glucose testing for patients with Type 1 diabetes, pediatric patients, or pregnant women.

Do not use sodium fluoride/potassium oxalate collection tubes as they may interfere with the results of the Atellica CH A1c_E assay.

A number of substances cause physiological changes in serum or plasma analyte concentrations. A comprehensive discussion of possible interfering substances, their serum or plasma concentrations, and their possible physiological involvements is beyond the scope of this document. Consult the listed reference for specific details on known potential interfering substances.[10]

As with any chemical reaction, you must be alert to the possible effect on results of unknown interferences from medications or endogenous substances. The laboratory and physician must evaluate all patient results in light of the total clinical status of the patient.

Expected Values

Reference Interval

A reference interval for healthy adults was established in accordance with CLSI Document EP28-A3c and verified on the Atellica CH Analyzer.[11]

Group	HbA1c (%)	HbA1c (mmol/mol)
Diabetic	≥ 6.5	≥ 48
Prediabetes	5.7–6.4	39–47
Normal	< 5.7	< 39

Siemens has verified the transference of reported reference range[12] for the Atellica CH A1c_E assay.[8]

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results. Consider these values as guidance only.[11]

Performance Characteristics

Measuring Interval

The Atellica CH A1c_E assay provides results from 3.80 %HbA1c (18.03 mmol/mol) to 14.00 %HbA1c (129.50 mmol/mol).

The assay range for A1c is 2.97–33.45 µmol/L (0.28–3.13 g/dL).

The assay range for tHb is 74.74–320.15 µmol/L (6.99–29.95 g/dL).

The system flags all values that are outside the specified measuring interval. If this occurs, remix the sample and repeat the analysis.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[13] The assay is designed to have a limit of blank (LoB) < 3.8% for %HbA1c, < 90 µmol/L for tHb, and < 3.0 µmol/L for A1c. The assay is designed to have a limit of detection (LoD) ≤ 3.8% for %HbA1c, ≤ 90 µmol/L for tHb, and ≤ 3.0 µmol/L for A1c.

Assay results obtained at individual laboratories may vary from the data presented.

The LoB is the highest measurement result that is likely to be observed on a blank sample. The LoD is the smallest amount that this assay can reliably detect to determine presence or absence of an analyte. The LoB and LoD for the Atellica CH A1c_E assay are shown below.

Limit	HbA1c (%)	tHb (µmol/L)	A1c (µmol/L)
LoB	3.11	61.38	1.65
LoD	3.53	65.54	2.39

The LoD corresponds to the lowest concentration of A1c or tHb that can be detected with a probability of 95%. The LoD was determined using 360 determinations, with 180 blank and 180 low level replicates. For %HbA1c determinations, these values were calculated based on a normal tHb value of 150 µmol/L (14 g/dL).

Precision

The repeatability precision of the Atellica CH A1c_E assay is designed to have the following characteristics:

- NGSP: 3.80–14.00% HbA1c with a CV% ≤ 1.5%
- IFCC: 18.03–129.50 mmol/mol with a CV% ≤ 3.0%

The within-lab precision of the Atellica CH A1c_E assay is designed to have the following characteristics:

- NGSP: 3.80–14.00% HbA1c with a CV% ≤ 2.0%
- IFCC: 18.03–129.50 mmol/mol with a CV% ≤ 5.0%

Precision was determined in accordance with CLSI Document EP05-A3.[14] Samples were assayed on an Atellica CH Analyzer in duplicate in 2 runs per day for 20 days (N ≥ 80 for each sample). Testing was performed using 3 lots of reagents on 3 systems for a total of 9 sets of data. Two calibrations were performed over the duration of the study. Data were analyzed using Analysis of Variance (ANOVA) consistent with CLSI document EP05-A3.[14] The pooled data from the study is shown in the tables below. The following results were obtained:

NGSP

			Repeatability		Within-Lab Precision	
Sample Type	N	Mean (%HbA1c)	SD[a] (%HbA1c)	CV[b] (%)	SD (%HbA1c)	CV (%)
Control 1	720	4.62	0.03	0.6	0.09	2.0
Control 2	720	8.94	0.03	0.3	0.10	1.2
MDP1 (5.0 %HbA1c)[c]	720	5.28	0.02	0.5	0.08	1.6
MDP2 (6.5 %HbA1c)	720	6.49	0.03	0.4	0.09	1.4
MDP3 (8.0 %HbA1c)	720	7.89	0.03	0.3	0.09	1.1
MDP4 (12.0 %HbA1c)	720	11.79	0.03	0.3	0.14	1.2

[a] Standard deviation.
[b] Coefficient of variation.
[c] MDP = Medical Decision Pool for the target %HbA1c listed.

IFCC

Sample Type	N	Mean (mmol/mol)	Repeatability SD[a] (mmol/mol)	Repeatability CV[b] (%)	Within-Lab Precision SD (mmol/mol)	Within-Lab Precision CV (%)
Control 1	720	26.97	0.28	1.0	1.03	3.8
Control 2	720	74.16	0.34	0.5	1.14	1.5
MDP1 (5.0 %HbA1c)[c]	720	34.14	0.27	0.8	0.91	2.7
MDP2 (6.5 %HbA1c)	720	47.45	0.29	0.6	1.00	2.1
MDP3 (8.0 %HbA1c)	720	62.70	0.28	0.4	0.96	1.5
MDP4 (12.0 %HbA1c)	720	105.39	0.33	0.3	1.54	1.5

[a] Standard deviation.
[b] Coefficient of variation.
[c] MDP = Medical Decision Pool for the target %HbA1c listed.

Assay results obtained at individual laboratories may vary from the data presented.

Assay Comparison

The Atellica CH A1c_E assay is designed to have a correlation coefficient of ≥ 0.950 and a slope of 1.0 ± 0.09 %HbA1c (NGSP) and 1.0 ± 0.010 mmol/mol (IFCC) when compared to the NGSP Reference Method. Assay comparison was determined using the Passing-Bablok and Deming linear regression model in accordance with CLSI Document EP09-A3.[15] The following results were obtained:

Passing-Bablok Regression

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
NGSP	NGSP Reference Method	y = 0.986x - 0.030 (%HbA1c)	4.00–13.60 (%HbA1c)	172	0.995
IFCC	NGSP Reference Method	y = 0.986x - 0.664 (mmol/mol)	20.20–125.14 (mmol/mol)	172	0.995

[a] Number of samples tested.
[b] Correlation coefficient.

Deming Regression

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
NGSP	NGSP Reference Method	y = 0.989x - 0.043 (%HbA1c)	4.00–13.60 (%HbA1c)	172	0.995
IFCC	NGSP Reference Method	y = 0.989x - 0.729 (mmol/mol)	20.20–125.14 (mmol/mol)	172	0.995

[a] Number of samples tested.
[b] Correlation coefficient.

The agreement of the assay may vary depending on the study design, comparative assay, and sample population. Assay results obtained at individual laboratories may vary from the data presented.

Anticoagulant Comparison

To confirm the equivalency of anticoagulants, the performance of the Atellica CH A1c_E assay was compared for 4 anticoagulants. Testing was performed on the Atellica CH Analyzer using one lot of reagents and a single replicate from a matched set of each of 3 anticoagulants (K_3-EDTA; sodium fluoride/Na_2 EDTA; and lithium heparin) and K_2-EDTA samples in accordance with CLSI document EP09-A3.[15]

Passing-Bablok Regression

Specimen Type (y)	Comparison Specimen (x)	N[a]	r[b]	Regression Equation
K_3-EDTA	K_2-EDTA	55	0.9997	y = 0.989x + 0.074 (%HbA1c)
Sodium Fluoride/Na_2 EDTA	K_2-EDTA	55	0.9997	y = 0.983x + 0.102 (%HbA1c)
Lithium Heparin	K_2-EDTA	55	0.9996	y = 1.022x - 0.023 (%HbA1c)

[a] Number of samples tested.
[b] Correlation coefficient.

Deming Regression

Specimen Type (y)	Comparison Specimen (x)	N[a]	r[b]	Regression Equation
K_3-EDTA	K_2-EDTA	55	0.9997	y = 0.990x + 0.059 (%HbA1c)
Sodium Fluoride/Na_2 EDTA	K_2-EDTA	55	0.9997	y = 0.996x + 0.088 (%HbA1c)
Lithium Heparin	K_2-EDTA	55	0.9996	y = 1.023x - 0.034 (%HbA1c)

[a] Number of samples tested.
[b] Correlation coefficient.

The correlation of the sample types may vary depending on the study design and sample population. Results obtained at individual laboratories may vary from the data provided.

Interferences

Hemolysis, Icterus, and Lipemia (HIL)

The Atellica CH A1c_E assay is designed to have ≤ 5% interference from hemoglobin, bilirubin, and lipemia. Interfering substances at the levels indicated in the table below were tested in accordance with CLSI Document EP07-A2 using the Atellica CH A1c_E assay.[16]

Bias is the difference in the results between the control sample (does not contain the interferent) and the test sample (contains the interferent) expressed in percent. Bias > 5% is considered interference. Analyte results should not be corrected based on this bias.

Substance[a]	Substance Test Concentration Common Units (SI Units)	Analyte Concentration (~ 6.5% HbA1c)	Percent Bias (~ 8.0% HbA1c)
Bilirubin, conjugated	10.0 mg/dL (118.6 µmol/L)	NSI[b]	NSI
Bilirubin, unconjugated	10.0 mg/dL (170.9 µmol/L)	NSI	NSI
Lipemia (Intralipid®)	1000 mg/dL (11.3 mmol/L)[c]	NSI	NSI

[a] Hemolysis is not applicable to hemoglobin testing.
[b] NSI = No significant interference. A percentage effect > 5% is considered a significant interference.
[c] As triolein.

Assay results obtained at individual laboratories may vary from the data presented.

Other Endogenous Substances

The following substances do not interfere with the Atellica CH A1c_E assay when present in human anticoagulated venous whole blood at the concentrations indicated in the table below. Bias due to these substances is ≤ 5% at an analyte concentration of ~ 6.5% HbA1c and ~ 8.0% HbA1c.[16]

	Substance Test Concentration Common Units (SI Units)	Analyte Concentration (~ 6.5% HbA1c)	Percent Bias (~ 8.0% HbA1c)
Triglycerides	2000 mg/dL (22.6 mmol/L)	NSI[a]	NSI
Total Protein	22 g/dL (222 g/L)	NSI	NSI
Ascorbic Acid	3.0 mg/dL (170.5 µmol/L)	NSI	NSI
Urea	667 mg/dL (111.06 mmol/L)	NSI	NSI

[a] NSI = No significant interference. A percentage effect > 5% is considered a significant interference.

Assay results obtained at individual laboratories may vary from the data presented.

Exogenous Substances

The following exogenous substances do not interfere with the Atellica CH A1c_E assay when present in samples at the concentrations indicated in the table below.[16]

	Substance Test Concentration Common Units (SI Units)	Analyte Concentration (~ 6.5% HbA1c)	Percent Bias (~ 8.0% HbA1c)
Acarbose	50 mg/dL (0.77 mmol/L)	NSI[a]	NSI
Acetaminophen	200 µg/mL (1323 µmol/L)	NSI	NSI
Acetylsalicylate	50.0 mg/dL (2.8 mmol/L)	NSI	NSI
Atorvastatin	600 µg Eq/L (600 µg Eq/L)	NSI	NSI
Captopril	0.5 mg/dL (23 µmol/L)	NSI	NSI
Chlorpropamide	74.7 mg/dL (2.7 mmol/L)	NSI	NSI
Cyanate	64.8 mg/dL (9.97 mmol/L)	NSI	NSI
Furosemide	6.0 mg/dL (181.3 µmol/L)	NSI	NSI
Gemfibrozil	7.5 mg/dL (300 µmol/L)	NSI	NSI
Glucose	1000 mg/dL (55 mmol/L)	NSI	NSI

	Substance Test Concentration Common Units (SI Units)	Analyte Concentration (~ 6.5% HbA1c)	Percent Bias (~ 8.0% HbA1c)
Ibuprofen	0.5 mg/mL (2427 µmol/L)	NSI	NSI
Insulin	450 µU/mL (450 µU/mL)	NSI	NSI
Losartan	5 mg/dL (0.11 mmol/L)	NSI	NSI
Metamizole	90 mg/dL (2.7 mmol/L)	NSI	NSI
Metformin	5.1 mg/dL (310 µmol/L)	NSI	NSI
N-acetylcysteine	5.1 mmol/L (5 mmol/L)	NSI	NSI
Nicotinic Acid	61 mg/dL (4.95 mmol/L)	NSI	NSI
Propranolol	0.2 mg/dL (7.71 µmol/L)	NSI	NSI
Repaglinide	60 ng/mL (132.57 nmol/L)	NSI	NSI
Rheumatoid Factor	200 IU/mL (200 IU/mL)	NSI	NSI
Vitamin E	8.6 mg/dL (200 µmol/L)	NSI	NSI

[a] NSI = No significant interference. A percentage effect > 5% is considered a significant interference.

Assay results obtained at individual laboratories may vary from the data presented.

Hemoglobin Variants

To assess the interference of hemoglobin variants on the performance of the Atellica CH A1c_E assay, anticoagulated human blood samples with known concentrations of hemoglobin variants and HbA1c were tested. The effect of each hemoglobin variant on assay performance was evaluated comparing the mean observed %HbA1c values obtained on the Atellica CH Analyzer to the mean expected %HbA1c values (provided by the supplier of the sample).

Hb Variant	N	Range (% Variant)	Range (%HbA1c)	Relative % Bias (Range % Bias) ~ 6% HbA1c	Relative % Bias (Range % Bias) ~ 9% HbA1c
HbC	37	24.6–39.4%	5.1–12.7%	-3.52% (-11.83–0.46)	-4.93% (-10.43–0.15)
HbD	27	32.7–41.3%	4.8–10.3%	-2.92% (-5.34–0.45)	-1.97% (-5.19–6.00)
HbE	21	21.7–40.5%	4.8–8.7%	-0.40% (-4.64–2.83)	0.28% (-2.39–2.36)
HbS	20	22.2–35.4%	5.4–15.2%	-2.02% (-5.62–-1.83)	-2.00% (-3.29–-0.80)

Hb Variant	N	Range (% Variant)	Range (%HbA1c)	Relative % Bias (Range % Bias) ~ 6% HbA1c	Relative % Bias (Range % Bias) ~ 9% HbA1c
HbA2	20	4.4–6.9%	4.9–10.8%	-2.14% (-7.10–2.79)	-1.36% (-2.54–-0.73)
HbF[a]	20	6.8–34.7%	5.4–8.9%	Bias > 5% N/A[b]	Bias > 5% N/A

[a] Refer to *Limitations*

[b] Not applicable.

Assay results obtained at individual laboratories may vary from the data presented.

Hemoglobin Derivatives

The interference effect of hemoglobin derivatives on the Atellica CH A1c_E assay was determined as described in CLSI document EP7-A2 on the Atellica CH Analyzer.[16] No significant interference was observed for HbA0, HbA1a, HbA1b and for the hemoglobin derivatives listed below. A percentage effect of > 5% is considered a significant interference.

- Acetylated hemoglobin with ≥ 50 mg/dL of acetylsalicylic acid
- Carbamylated hemoglobin with ≥ 10 mmol/L of cyanate
- Labile hemoglobin with ≥ 1000 mg/dL of glucose

Standardization

The Atellica CH A1c_E assay standardization is traceable to the IFCC reference calibrators.

Technical Assistance

For customer support, contact your local technical support provider or distributor.

siemens.com/healthineers

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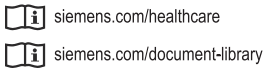
Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
	Version of instructions for use
	Internet URL address to access the electronic instructions for use
Rev. REVISION	Revision
	Caution Consult instructions for use or accompanying documents for cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device.
	Biological risks Potential biological risks are associated with the medical device.

Symbol	Symbol Title and Description
	Corrosive
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.
	Up Store in an upright position.
	Do not freeze
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Handheld barcode scanner
	*In vitro* diagnostic medical device
	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.

Symbol	Symbol Title and Description
RxOnly	Prescription device (US only) Applies only to United States-registered IVD assays. CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.
	Mixing of substances Mix product before use.
	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
EC REP	Authorized Representative in the European Community
	Use-by date Use by the designated date.
LOT	Batch code
REF	Catalog number
	Recycle
	Printed with soy ink
CE	CE Mark
CE 0088	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year-month-day)
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
UNITS C	Common Units
UNITS SI	International System of Units
MATERIAL	Material
MATERIAL ID	Unique material identification number

Symbol	Symbol Title and Description
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

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