HEMOGLOBIN A1c

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

WARNING: The Hemoglobin A1c assay has significant interference with the fetal hemoglobin (HbF). Hemoglobin A1c results are invalid for patients with abnormal amounts of HbF, including those with known Hereditary Persistence of Fetal Hemoglobin. For more information regarding the specific concentrations of HbF that were found to interfere with Hemoglobin A1c assay, refer to the SPECIFIC PERFORMANCE CHARACTERISTICS, Specificity section of this package insert.

Read Highlighted Changes: Revised May 2022.

en

Hemoglobin A1c

REF 4P52-20

G11016R05

B4P5C0

FOR USE WITH

ARCHITECT

INTENDED USE

The Hemoglobin A1c assay is used in clinical laboratories for the quantitative *in vitro* measurement of percent hemoglobin A1c (NGSP) or HbA1c fraction mmol/mol (IFCC) in human whole blood and hemolysate on the ARCHITECT *c* 8000 and *c* 4000 Systems.
Hemoglobin A1c measurements are used as an aid in the diagnosis of diabetes mellitus, as an aid to identify patients who may be at risk for developing diabetes mellitus, and for the monitoring of long-term blood glucose control in individuals with diabetes mellitus.

SUMMARY AND EXPLANATION OF TEST

HbA1c is the fraction of hemoglobin A that is first reversibly, then irreversibly glycated at one or both *N*-terminal valines of the β-chain.[1] The longer red blood cells are in circulation and the higher the ambient glucose levels, the higher the concentration of HbA1c. HbA1c reflects the average blood glucose level during the preceding 2 to 3 months. The HbA1c assay is useful as an aid in the:

- diagnosis of diabetes mellitus,
- identification of patients at risk for developing diabetes, and
- monitoring of patients with diabetes mellitus.[2-6]

For monitoring diabetic patients, it is recommended that glycemic goals are individualized following current professional society recommendations.[7] As recommended by the American Diabetes Association (ADA), patients in the range of 5.7 - 6.4 %HbA1c (39 - 46 mmol/mol) would be in the category of increased risk for diabetes and results ≥ 6.5% (48 mmol/mol) may aid in the diagnosis of diabetes.[7]
Several studies, including the Diabetes Control and Complications Trial (DCCT), have shown that long-term control of diabetes can prevent complications such as cardiovascular disease, retinopathy, nephropathy, and neuropathy. Measurement of HbA1c can be invaluable in the monitoring of glycemic control of diabetic patients.[8-10]
This method is certified by the National Glycohemoglobin Standardization Program (NGSP), standardized to International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and traceable to DCCT.

PRINCIPLES OF PROCEDURE

The Hemoglobin A1c assay consists of two separate concentration measurements: glycated hemoglobin (HbA1c) and total hemoglobin (THb). The two concentrations are used to determine the percent HbA1c (NGSP units) or the hemoglobin fraction in mmol/mol (IFCC units).
The individual concentration values of HbA1c and THb generated by the Hemoglobin A1c assay are used only for calculating the percent hemoglobin A1c or HbA1c fraction, and must not be used individually for diagnostic purposes.
The anticoagulated whole blood specimen is lysed automatically on the system for the Whole Blood application or may be lysed manually using the Hemoglobin A1c Diluent (A1cDIL) for the Hemolysate application.

Glycated Hemoglobin (HbA1c)

The Hemoglobin A1c assay utilizes an enzymatic method that specifically measures *N*-terminal fructosyl dipeptides of the β-chain of HbA1c.

- In the pretreatment process, the erythrocytes are lysed and the hemoglobin is transformed to methemoglobin by reaction with sodium nitrite.
- With the addition of Reagent 1 (R1) to the sample, the glycosylated *N*-terminal dipeptide (fructosyl-VH) of the β-chain of hemoglobin is cleaved by the action of protease. The hemoglobin is transformed to stable methemoglobin azide by the action of sodium azide and the concentration of the hemoglobin is determined by measuring absorbance.
- Addition of Reagent 2 (R2) starts a reaction and fructosyl peptide oxidase (FPOX) is allowed to react with fructosyl-VH. The HbA1c concentration is measured by determining the resultant hydrogen peroxide.

Total Hemoglobin (THb)

The hemoglobin is oxidized to stable methemoglobin azide by the action of sodium nitrite and sodium azide and the concentration of the hemoglobin is determined by measuring absorbance (sample + R1).

Hemoglobin A1c Calculations[11]

The final result is expressed as %HbA1c (NGSP) or mmol/mol HbA1c (IFCC) and is automatically calculated by the system from the HbA1c/THb ratio as follows:

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

%HbA1c DCCT/NGSP:
HbA1c (%) = IFCC x 0.09148 + 2.152

Methodology: Enzymatic

REAGENTS

Reagent Kit

REF 4P52-20 Hemoglobin A1c is supplied as a liquid, ready-to-use, three-reagent kit which contains:

R1	Reagent 1	1 x 52 mL
R2	Reagent 2	1 x 20 mL
A1cDIL	Diluent	2 x 35 mL

Estimated tests per kit: 300
Calculation is based on the minimum reagent fill volume per kit.

Reactive	Ingredients	Concentration
R1	10-(carboxymethylaminocarbonyl)-3,7-bis(dimethylamino) phenothiazine sodium salt	0.000817%
	Protease (Bacterial)	< 1 MU/dL
R2	Peroxidase (Horseradish)	5 to 15 kU/dL
	Fructosyl-peptide-oxidase (*E. coli,* recombinant)	300 to 900 U/dL
A1cDIL	Sodium nitrite	> 0.05 to < 0.3%

Inactive Ingredients: R1 contains sodium azide as a stabilizer and preservative. R1 and A1cDIL contain ProClin 300 as a preservative. R2 contains ofloxacin as a preservative.

REAGENT HANDLING AND STORAGE

Reagent Handling

- R1, R2, and A1cDIL are ready for use.
- Remove air bubbles, if present in the reagent cartridge, with a new applicator stick. Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate. To minimize volume depletion, do not use a transfer pipette to remove the bubbles.

  CAUTION: Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration that could impact results.

Reagent Storage

- Unopened reagents are stable until the expiration date when stored at 2 to 8°C.
- Reagent stability is 50 days (1,200 hours) if the reagent is uncapped and on board.
- When either the R1 or R2 reagent cartridge becomes empty, replace both cartridges.
- A1cDIL can be replaced independently of R1 and R2.

Indications of Deterioration

Instability or deterioration should be suspected if there are visible signs of leakage, extreme turbidity, microbial growth, or if control values fall outside the acceptance criteria.

WARNINGS AND PRECAUTIONS

Precautions for Use

- IVD
- For *In Vitro* Diagnostic Use.
- Rx ONLY
- Do not use components beyond the expiration date.
- Do not mix R1 and R2 from different kit lot numbers.
  Note: A1cDIL may be used with R1 and R2 from different kit lot numbers.
- **WARNING:** Do not use ARCHITECT sample cups for whole blood samples. Refer to the Assay Procedure section of this package insert for further information.
- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human-sourced materials be considered potentially infectious and handled in accordance with the OSHA Standard on Bloodborne Pathogens.[12] Biosafety Level 2[13] or other appropriate biosafety practices[14,15] should be used for materials that contain or are suspected of containing infectious agents.

The following warnings and precautions apply to: R1	
	
DANGER:	Contains N,N-dimethylformamide, methylisothiazolones, diethylenetriamine-pentaacetic acid, morpholinoethanesulfonic acid, monohydrate* and sodium azide.
H360	May damage fertility or the unborn child.
H317	May cause an allergic skin reaction.
H316*	Causes mild skin irritation.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P201	Obtain special instructions before use.
P261	Avoid breathing mist / vapors / spray.
P280	Wear protective gloves / protective clothing / eye protection.
P272	Contaminated work clothing should not be allowed out of the workplace.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
P308+P313	IF exposed or concerned: Get medical advice / attention.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

* Not applicable where regulation EC 1272/2008 (CLP) or OSHA Hazard Communication 29 CFR 1910.1200 (HCS) 2012 have been implemented.

The following warnings and precautions apply to: R2	
WARNING:	Contains citric acid*.
H316*	Causes mild skin irritation.
P333+P313*	If skin irritation or rash occurs: Get medical advice / attention.

* Not applicable where regulation EC 1272/2008 (CLP) or OSHA Hazard Communication 29 CFR 1910.1200 (HCS) 2012 have been implemented.

The following warnings and precautions apply to: A1cDIL	
	
WARNING:	Contains maleic acid, methylisothiazolones and sodium nitrite*.
H317	May cause an allergic skin reaction.
H402*	Harmful to aquatic life.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
P273*	Avoid release to the environment.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P302+P352	IF ON SKIN: Wash with plenty of water.
P333+P313	If skin irritation or rash occurs: Get medical advice / attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

* Not applicable where regulation EC 1272/2008 (CLP) or OSHA Hazard Communication 29 CFR 1910.1200 (HCS) 2012 have been implemented.

Follow local chemical disposal regulations based on your location along with recommendations and content in the Safety Data Sheet to determine the safe disposal of this product.

For the most current hazard information, see the product Safety Data Sheet.

Safety Data Sheets are available at www.corelaboratory.abbott or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to *Section 8* of the **ARCHITECT System Operations Manual**.

SPECIMEN COLLECTION AND HANDLING

Suitable Specimens

- Use only whole blood specimens collected by standard venipuncture techniques into plastic tubes. Acceptable anticoagulants are:
  - Dipotassium EDTA
  - Lithium heparin
  - Sodium heparin
  - Sodium fluoride/disodium EDTA
  - Tripotassium EDTA

Preparation for Analysis

- Follow the tube manufacturer's collection instructions for specimen collection tubes.
- Do not overfill specimen collection tubes. Whole blood samples greater than 78 mm in height from the bottom of tube will result in an instrument error and results will not be generated. Refer to *Section 10* of the **ARCHITECT System Operations Manual**.
- For testing whole blood samples less than 600 µL, use 12 x 75 mm polypropylene conical bottom tubes.
- **Do not centrifuge samples.**
- Visually inspect the specimens. If fibrin clots or particulate matter is observed, remove with a clean applicator stick.
- Mix all specimens thoroughly by low speed vortexing or gently inverting 10 times prior to loading onto the ARCHITECT *c* System.
- Frozen specimens must be completely thawed prior to mixing. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.

Specimen Storage

- Analyze fresh specimens if possible. If testing will be delayed, store specimens per the instructions below.

Whole Blood

- Specimens may be stored for:
  - up to 8 hours at room temperature or
  - up to 7 days at 2 to 8°C

  NOTE: Refer to the Suitable Specimens section of this package insert.
- If testing will be delayed more than 7 days, store at -70°C or colder.
  CAUTION: Whole blood specimens that require freezing must be stored at -70°C or colder.
- Avoid more than one freeze/thaw cycle.
- **NOTE:** During storage, specimens may settle. It is good laboratory practice to mix specimens thoroughly prior to loading onto the system.

Hemolysate

- Hemolyzed specimens may be stored for
  - up to 4 hours at room temperature or
  - up to 24 hours at 2 to 8°C.

  NOTE: Refer to the Suitable Specimens section of this package insert.
- Do not freeze hemolyzed specimens.
- **NOTE:** During storage, hemolyzed specimens may settle. It is good laboratory practice to mix specimens thoroughly prior to loading onto the system.

PROCEDURE

Materials Provided

REF 4P52-20 Hemoglobin A_{1c} Reagent Kit

Materials Required but not Provided

- REF 4P52-01 Hemoglobin A_{1c} Calibrators
- REF 4P52-02 Hemoglobin A_{1c} Calibrators

  The concentration of each calibrator is value-assigned and can change for each lot manufactured. Refer to the Hemoglobin A_{1c} Calibrator Value Sheet.
- REF 4P52-10 Hemoglobin A_{1c} Controls*
- REF 4P52-11 Hemoglobin A_{1c} Controls*

  The concentration of each control is value-assigned with NGSP and IFCC values and can change for each lot manufactured. Refer to the Hemoglobin A_{1c} Control Value Sheet.
- Commercially available whole blood controls**
- 12 x 75 mm polypropylene conical bottom tubes**
- Calibrated adjustable pipette capable of measuring 222 µL*
- Calibrated micropipette capable of measuring 10 µL*
- REF 01G48-04 *c* 4000/*c* 8000 Sample Probe
- Vortex (optional)

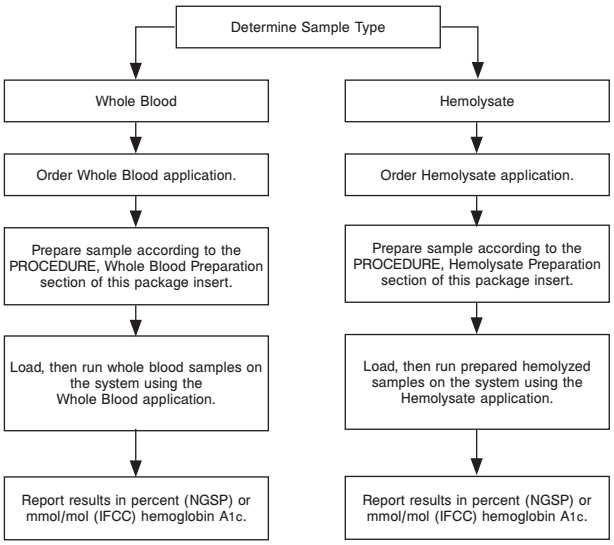
* Hemolysate application
** Whole Blood application

Assay Procedure

1. Load the R1, R2, and A1cDIL on the ARCHITECT *c* 8000 or *c* 4000 System.
   - Place the A1cDIL in the reagent supply center (R1 - *c* 8000) for the Whole Blood application.
   - Configure the A1cDIL in the Configure Reagent Settings screen by selecting *New*, then *Configure F6*. Enter the reagent name as *A_{1c}DIL*, the reagent type as *Sample Diluent*, the A1cDIL lot number and serial number as shown on the A1cDIL bottle label, and the R1 cartridge size as *Small (55 mL cartridge)*. Select *Add kit*.
   - Assign the location of the A1cDIL. Refer to **Load non-bar coded reagents** in *Section 5* of the **ARCHITECT System Operations Manual**.
2. Perform a calibration for the Whole Blood and/or the Hemolysate application(s) as needed. Refer to *Section 6* of the **ARCHITECT System Operations Manual**.
3. Refer to the flowchart below.

   NOTE: No more than one replicate can be sampled from a sample cup or tube. To minimize the effects of evaporation, verify adequate sample volume is present before running the test.

   For information on ordering patient samples and controls, refer to *Section 5* of the **ARCHITECT System Operations Manual**.



Whole Blood Preparation

- **WARNING: Do not use ARCHITECT sample cups.**
- **WARNING: Do not overfill specimen collection tubes. Whole blood samples greater than 78 mm in height from the bottom of tube will result in an instrument error and results will not be generated. Refer to *Section 10* of the ARCHITECT System Operations Manual.**
- Select the appropriate sample vessel using the table below:

If sample is:	Then:
	Do not use the Whole Blood application.
< 200 µL	Follow the instructions in the PROCEDURE, Hemolysate Preparation section of this package insert.
200 µL - 600 µL	Use 12 x 75 mm polypropylene conical bottom tubes only.
> 600 µL	Use suitable tubes or polypropylene conical bottom tubes.
> 78 mm in height in a large tube	Pipette 600 µL of sample into a suitable tube or polypropylene conical bottom tube.

Hemolysate Preparation

- The minimum sample volume requirement is 150 µL for ARCHITECT sample cups.
- Prepare the hemolysate samples as follows:
  1. Using a calibrated pipette, dispense 222 µL A1cDIL into a tube or sample cup.
  2. Using a calibrated micropipette, withdraw 10 µL of the well-mixed whole blood patient specimen.
  3. Wipe excess blood from the exterior of the pipette to ensure accurate transfer of the sample.
  4. Insert the pipette into the tube or sample cup containing the A1cDIL allowing the tip of the pipette to just make contact with the surface of the A1cDIL and dispense the 10 µL sample (1:23.2 dilution).
  5. Withdraw and dispense twice to rinse the pipette, always keeping the tip of the pipette in contact with the fluid in the tube.
  6. Mix hemolysate thoroughly by low speed vortexing or by gently inverting 10 times. Avoid foaming.
  7. Allow the hemolysate to stand for a minimum of 1 minute at room temperature prior to testing.
  8. If the hemolysate is prepared in a tube, transfer to a sample cup and place the cup on the instrument.

  NOTE: The number of tests per kit is based on the 222 µL of A1cDIL and 10 µL of specimen volumes stated in steps 1 and 2 above. However, alternate volumes may be used for the 1:23.2 dilution, such as 555 µL of A1cDIL and 25 µL of specimen.

Specimen Dilution Procedure

Specimens must not be diluted since the result is a calculated ratio. Refer to the RESULTS section of this package insert.

CALIBRATION

- Calibration is stable for approximately 50 days (1,200 hours) and is required with each change in reagent lot number. Verify calibration with all levels of controls. If control results fall outside acceptable ranges, recalibration may be necessary.
- Both the Whole Blood and Hemolysate applications use the Hemoglobin A_{1c} Calibrators (REF 4P52-01 and 4P52-02), which are supplied separately.
- Hemoglobin A_{1c} Calibrators are traceable to NGSP and IFCC reference methods.
- To perform a calibration, follow the instructions provided in the calibrator package insert.

QUALITY CONTROL

The following is the recommendation of Abbott Laboratories for quality control. As appropriate, refer to your laboratory standard operating procedure(s) and/or quality assurance plan for additional quality control requirements and potential corrective actions.

- Two levels of controls are to be run every 24 hours. The Hemoglobin A_{1c} assay uses:
  - Commercially available whole blood controls for the Whole Blood application. Follow the manufacturer's instructions for preparation of commercially available whole blood controls.
  - Hemoglobin A_{1c} Controls (REF 4P52-10 and 4P52-11) for the Hemolysate application. Refer to the Hemoglobin A_{1c} Control Value Sheet for NGSP and IFCC ranges.
- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, patient values may be suspect and corrective action should be taken. Follow the established quality control procedures for your laboratory. Recalibration may be necessary.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

RESULTS

- The individual concentrations of the Whole Blood and Hemolysate applications are measured by the system.

  NOTE: HbA_{1c} or THb concentrations must not be used individually for clinical purposes.

  IMPORTANT: Assay parameters must be configured exactly as defined in the ASSAY PARAMETERS section of this package insert.
- Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert.

Conventional Units (NGSP)

The percent HbA_{1c} (%HbA_{1c}) is automatically calculated by the system per the calculation provided in the Hemoglobin A_{1c} Calculations section.

SI Units (IFCC)

The hemoglobin A_{1c} fraction (mmol/mol HbA_{1c}) is automatically calculated by the system per the calculation provided in the Hemoglobin A_{1c} Calculations section.

LIMITATIONS OF THE PROCEDURE

- For use with ARCHITECT System software v8.1 or higher.
- The Hemoglobin A_{1c} assay must not be used on the ARCHITECT *c* 16000 System.
- This assay must be performed by qualified laboratory personnel, under appropriate laboratory conditions, solely for the intended use of the assay.
- Do not centrifuge samples.
- Do not freeze specimens that have been hemolyzed with the A1cDIL.
- Whole blood specimens that require freezing must be stored at -70°C or colder.
- Do not overfill specimen collection tubes. Whole blood samples greater than 78 mm in height from the bottom of tube will result in an instrument error and results will not be generated. Refer to *Section 10* of the **ARCHITECT System Operations Manual**.
- Whole blood samples cannot be run in sample cups.
- Use specimen collection tubes, or for sample volumes < 600 µL use the 12 x 75 mm polypropylene conical bottom tubes as recommended in the PROCEDURE, Materials Required but not Provided section of this package insert.
- WARNING: The Hemoglobin A_{1c} assay should not be used to diagnose diabetes during pregnancy. Hemoglobin A_{1c} reflects the average blood glucose levels over the preceding 3 months (*i.e.*, 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.[16-19]
- Blood transfusions may impact HbA_{1c} concentration in the patient sample.
- The Hemoglobin A_{1c} assay should not be used to diagnose or monitor diabetes in patients with the following conditions:[16-19]
  - hemoglobinopathies except as demonstrated to produce acceptable performance (*e.g.*, sickle cell trait - refer to the SPECIFIC PERFORMANCE CHARACTERISTICS section of this package insert)
  - abnormal red blood cell turnover (*e.g.*, 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 HbA_{1c} 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.
- This test should not replace glucose testing for patients with Type 1 diabetes, pediatric patients, or pregnant women.
- The Hemoglobin A_{1c} assay is susceptible to interference effects from conjugated bilirubin at > 15.0 mg/dL (180 µmol/L) and unconjugated bilirubin at > 10.0 mg/dL (171 µmol/L).
- The observed bias for samples containing HbC, HbD, HbE, HbS and HbA_2 may be impacted by the method used to determine the reference Hemoglobin A_{1c} concentration.
- Glycated HbF is not detected by the assay as it does not contain the β-chain that characterizes HbA_{1c}. However, HbF is measured in the total Hb assay and as a consequence, specimens containing high amounts of HbF (> 5%) may result in lower than expected mmol/mol HbA_{1c} values (IFCC) and %HbA_{1c} values (NGSP).
- Refer to the SPECIMEN COLLECTION AND HANDLING section of this package insert for specimen limitations.

EXPECTED VALUES

For monitoring diabetic patients, it is recommended that glycemic goals are individualized following current professional society recommendations.[7] The American Diabetes Association (ADA) recommendations[7] are summarized in the following table.

HbA_{1c} Value	Glycemic Goal
< 8 %HbA_{1c} (64 mmol/mol)	Less stringent
< 7 %HbA_{1c} (53 mmol/mol)	General (non-pregnant adults)
< 6.5 %HbA_{1c} (48 mmol/mol)	More stringent

HbA_{1c} values above 6.5 %HbA_{1c} (48 mmol/mol) are an indication of hyperglycemia during the preceding 2 to 3 months or longer. According to the recommendations of the ADA, HbA_{1c} values above 6.5 %HbA_{1c} (48 mmol/mol) are suitable for the diagnosis of diabetes mellitus. Patients with HbA_{1c} values in the range of 5.7 - 6.4 %HbA_{1c} (39 - 46 mmol/mol) may be at a risk of developing diabetes.[3,20]

SPECIFIC PERFORMANCE CHARACTERISTICS

Measuring Interval

The measuring interval of the Hemoglobin A_{1c} assay is 4.0 to 14.0 %HbA_{1c} (20.22 to 129.51 mmol/mol HbA_{1c}).

Limit of Blank and Limit of Detection

Using a typical hemoglobin concentration of 8.2 mmol/L (13.2 g/dL) for the THb, the Hemoglobin A_{1c} LoB result is 2.51 %HbA_{1c} (3.89 mmol/mol) and LoD result is 2.52 %HbA_{1c} (4.05 mmol/mol).

Limit of Blank (LoB) and Limit of Detection (LoD) were determined for each of the Hemoglobin A_{1c} constituent assays (HbA_{1c} and THb) using National Committee for Clinical Laboratory Standards (NCCLS) protocol EP17-A.[21]

The HbA_{1c} constituent assay had an LoB of 31.9005 µmol/L and an LoD of 33.2230 µmol/L. The THb constituent assay had an LoB of 129.5129 µmol/L and an LoD of 295.5947 µmol/L.

Linearity

Linearity was verified using NCCLS protocol EP6-A.[22]

IFCC

The Hemoglobin A_{1c} assay is linear across the range of 20.22 to 129.51 mmol/mol HbA_{1c} based on an allowable tolerance of within or equal to ± 7%.

NGSP

The Hemoglobin A_{1c} assay is linear across the range of 4.0 to 14.0 %HbA_{1c} based on an allowable tolerance of within or equal to ± 5%.

Specificity

Hemoglobin Derivatives

A specificity study was conducted using Clinical and Laboratory Standards Institute (CLSI) protocol EP07-A2.[23] Specificity was assessed by comparing test samples containing the potential interferents listed below to reference samples. No interference was observed for:

- Acetylated Hemoglobin with ≥ 50 mg/dL of ASA (aspirin)
- Carbamylated Hemoglobin with ≥ 10 mmol/L of Cyanate
- Labile Hemoglobin with ≥ 1000 mg/dL of Glucose

IFCC

The Hemoglobin A_{1c} assay had a difference within ± 7% for samples with concentrations ≥ 38.78 mmol/mol HbA_{1c}.

NGSP

The Hemoglobin A_{1c} assay had a difference within ± 5% for samples with concentrations ≥ 5.7 %HbA_{1c}.

Hemoglobin Variants

A specificity study was conducted using CLSI protocol EP07-A2.[23] Specificity was assessed by comparing the Hemoglobin A_{1c} values to reference values for samples containing abnormal hemoglobins. Heterozygous hemoglobin variants (HbAS, HbAC, HbAD, HbAE, HbA_2) do not interfere with the Hemoglobin A_{1c} assay.

For the ARCHITECT *c* 8000 System, the data in %HbA_{1c} (NGSP) are summarized in the following table.

Hemoglobin Variant	Relative % Difference from Reference Concentration	
	~ 6.0 %HbA_{1c}	~ 9.0 %HbA_{1c}
HbC	-1.6	-1.9
HbD	-0.8	1.8
HbE	0.0	4.3
HbS	-1.4	4.7
HbA_2	-0.6	-0.5
HbF	Difference exceeds -5% when the amount of HbF in the sample exceeds 5%[a]	

[a] A negative % difference with HbF is proportional in magnitude to the % HbF present in the sample. For example, when the amount of HbF in the sample was 21.5%, the % difference was -18.5% on the ARCHITECT *c* 8000 System. Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert for further information.

NOTE: The presence of multiple variants in a sample may impact the % difference.

For the ARCHITECT *c* 4000 System, the data in %HbA1c (NGSP) are summarized in the following table.

Hemoglobin Variant	Relative % Difference from Reference Concentration			
	~ 6.0 %HbA1c (5.5 to 6.5 %HbA1c)		~ 9.0 %HbA1c (7.5 to 10.5 %HbA1c) [a]	
	Relative % Difference	Range [b]	Relative % Difference	Range [b]
HbC	-3.1	-6.9, 3.3	-0.5	-4.2, 2.7
HbD	0.6	-3.4, 3.2	0.2	-1.3, 2.6
HbE	1.0	-3.3, 7.8	2.5	-2.1, 6.3
HbS	-0.8	-3.6, 3.3	-0.5	-3.8, 2.2
HbA2	0.7	0.0, 1.7	2.9	1.4, 4.5
HbF	Difference exceeds -5% when the amount of HbF in the sample exceeds 5% [c]			

[a] The HbA2 results at ~ 9.0 %HbA1c consisted of samples between 7.2 to 11.2 %HbA1c.

[b] The range is defined as the minimum and maximum relative % difference at each concentration level (~ 6.0 and ~ 9.0 %HbA1c).

[c] A negative % difference with HbF is proportional in magnitude to the % HbF present in the sample. For example, when the amount of HbF in the sample was 20.4%, the % difference was -20.0% on the ARCHITECT *c* 4000 System. Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert for further information.

NOTE: The presence of multiple variants in a sample may impact the % difference.

Interference

Interference studies were conducted using CLSI protocol EP07-A2.[23] Interference effects were assessed by comparing test samples containing the potential interferents listed below to reference samples.

IFCC

The Hemoglobin A1c assay had a difference within ± 7% for samples with concentrations ≥ 38.78 mmol/mol HbA1c.

NGSP

The Hemoglobin A1c assay had a difference within ± 5% for samples with concentrations ≥ 5.7 %HbA1c.

For the ARCHITECT *c* 8000 and *c* 4000 Systems, the data in %HbA1c (NGSP) are summarized in the following tables.

Potential Interferent	Interferent Concentration		% Interference [a]			
			6.0 - 7.0 %HbA1c		≥ 8.0 %HbA1c	
			ARCHITECT *c* System			
	Conventional Units	SI Units	A [b]	B [b]	A [b]	B [b]
Ascorbic Acid	3.0 mg/dL	0.15 mmol/L	0.0	0.0	0.0	0.0
Bilirubin (Conjugated) [c]	15.0 mg/dL	180 µmol/L	-3.2	-3.1	-2.2	-3.3
Bilirubin (Unconjugated) [d]	10.0 mg/dL	171 µmol/L	-3.0	-2.3	-2.2	-2.7
Glucose	1000 mg/dL	55.5 mmol/L	0.0	0.0	0.0	0.0
Rheumatoid Factor	200 IU/mL	200 IU/mL	0.0	0.0	0.0	0.0
Triglycerides	3000 mg/dL	33.9 mmol/L	-1.6	0.0	0.0	-4.5
Total Protein	22 g/dL [e]	220 g/L	0.0	0.0	0.0	-1.1
Urea	667 mg/dL	111.06 mmol/L	0.0	0.0	0.0	0.0
Vitamin E	8.6 mg/dL	200 µmol/L	0.0	1.6	0.0	0.0

[a] $\% \text{ Interference} = \frac{\text{Test Result - Control Result}}{\text{Control Result}} \times 100$

[b] A = ARCHITECT *c* 8000 System; B = ARCHITECT *c* 4000 System

[c] Samples containing conjugated bilirubin at > 15.0 mg/dL (180 µmol/L) demonstrated interference. Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert for further information.

[d] Samples containing unconjugated bilirubin at > 10.0 mg/dL (171 µmol/L) demonstrated interference. Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert for further information.

[e] The total protein concentration of 22 g/dL includes serum protein as well as hemoglobin.

Potential Interferent	Interferent Concentration		% Interference [a]			
			6.0 - 7.0 %HbA1c		≥ 8.0 %HbA1c	
			ARCHITECT *c* System			
	Conventional Units	SI Units	A [b]	B [b]	A [b]	B [b]
Acarbose	50 mg/dL	0.77 mmol/L	0.0	0.0	0.0	0.0
Acetaminophen	200 µg/mL	1324 µmol/L	-0.24	-0.59	-0.80	-0.63
N-acetyl-4-benzoquinone imine	20 mg/L	134.2 µmol/L	-1.3	-1.5	-0.8	-0.8
N-acetyl-L-cysteine	1600 mg/L	9816 µmol/L	-2.6	-3.4	-2.5	-2.7
Acetylsalicylate	50.8 mg/dL	2.82 mmol/L	0.0	0.0	0.0	0.0
Atorvastatin	0.06 mg/dL	600 µg Eq/L	0.0	1.6	0.0	0.0
Captopril	0.5 mg/dL	23 µmol/L	-1.5	0.0	-1.1	0.0
Chlorpropamide	74.7 mg/dL	2.7 mmol/L	0.0	0.0	0.0	-1.1
Cyanate	50 mg/dL	6.16 mmol/L	0.0	0.0	1.1	1.1
Dipyrone	100 mg/L	300.3 µmol/L	0.1	0.2	0.1	0.1
Furosemide	6.0 mg/dL	181 µmol/L	0.0	0.0	0.0	1.1
Gemfibrozil	7.5 mg/dL	300 µmol/L	0.0	0.0	0.0	0.0
Ibuprofen	50 mg/dL	2425 µmol/L	0.0	0.0	0.0	1.1
Insulin	450 micro units per mL	450 micro units per mL	0.0	0.8	0.0	0.0
Losartan	5 mg/dL	0.11 mmol/L	0.0	0.0	0.0	0.0
Metformin	5.1 mg/dL	310 µmol/L	0.0	0.0	0.0	0.0
Nicotinic Acid	61 mg/dL	4.95 mmol/L	0.0	-1.5	0.0	-0.5
Propranolol	0.2 mg/dL	7.71 µmol/L	0.0	0.0	0.0	-0.5
Repaglinide	0.006 mg/dL	132.57 nmol/L	0.0	0.8	0.0	0.0
4-acetamido antipyrine	40 mg/L	163.3 µmol/L	-0.4	-0.2	-0.4	-0.0
4-aminoantipyrine	40 mg/L	197.0 µmol/L	-0.4	-0.3	-0.2	0.1
4-formylamino antipyrine	40 mg/L	173.2 µmol/L	-0.1	-0.1	-0.1	-0.6
4-methylamino antipyrine	40 mg/L	184.3 µmol/L	-0.3	-0.1	-0.4	-0.3

[a] $\% \text{ Interference} = \frac{\text{Test Result - Control Result}}{\text{Control Result}} \times 100$

[b] A = ARCHITECT *c* 8000 System; B = ARCHITECT *c* 4000 System

Refer to the LIMITATIONS OF THE PROCEDURE section of this package insert for further information.

Precision

A study was performed based on guidance from the NCCLS protocol EP5-A2.[24] Testing was conducted using 3 lots of Hemoglobin A1c Reagents and Calibrators, 1 lot of commercially available controls, and 3 instruments. Two levels of controls and 3 levels of human whole blood panels were assayed in a minimum of 2 replicates at 2 separate times per day for 20 different days. Each reagent lot used a stored calibration curve throughout the study.

IFCC

The Hemoglobin A1c assay is designed to have an imprecision of an SD of ≤ 1.42 mmol/mol HbA1c for samples with concentrations < 38.78 mmol/mol HbA1c, a ≤ 3% within-laboratory (total) %CV for samples targeted to 47.53 mmol/mol HbA1c (38.78 to 53.00 mmol/mol HbA1c, inclusive), and a ≤ 5.0% within-laboratory (total) %CV for samples with concentrations > 53.00 mmol/mol HbA1c.

NGSP

The Hemoglobin A_{1c} assay is designed to have an imprecision of an SD of ≤ 0.13 %HbA_{1c} for samples with concentrations < 5.7 %HbA_{1c}, a ≤ 2% within-laboratory (total) %CV for samples targeted to 6.5 %HbA_{1c} (5.7 to 7.0 %HbA_{1c}, inclusive), and a ≤ 3.5% within-laboratory (total) %CV for samples with concentrations > 7.0 %HbA_{1c}. For the ARCHITECT *c* 8000 System, the data in %HbA_{1c} (NGSP) are summarized in the following table.

Sample	Instrument	n	Mean %HbA_{1c}	Within-Run		Within-Laboratory Precision (Total)[a]		Precision with Additional Component of Between-Lot[b]	
				SD	%CV	SD	%CV	SD	%CV
Control 1	1	240	4.9	0.01	0.3	0.02	0.5	0.03	0.5
	2	240	4.9	0.01	0.3	0.02	0.4	0.02	0.4
	3	240	4.8	0.02	0.4	0.03	0.6	0.03	0.6
Control 2	1	240	9.6	0.03	0.3	0.04	0.4	0.09	1.0
	2	239[c]	9.6	0.03	0.3	0.04	0.4	0.08	0.9
	3	240	9.5	0.03	0.3	0.04	0.4	0.11	1.1
Panel Near 4.0 %HbA_{1c}	1	240	4.4	0.01	0.3	0.02	0.4	0.03	0.7
	2	240	4.4	0.01	0.3	0.02	0.4	0.03	0.7
	3	240	4.4	0.02	0.3	0.02	0.5	0.03	0.6
Panel Range 6.0 - 7.0 %HbA_{1c}	1	240	6.4	0.01	0.2	0.02	0.4	0.05	0.7
	2	240	6.4	0.02	0.3	0.02	0.3	0.04	0.6
	3	240	6.4	0.02	0.2	0.03	0.5	0.04	0.6
Panel Range 8.0 - 10.0 %HbA_{1c}	1	240	8.9	0.02	0.2	0.03	0.3	0.06	0.7
	2	240	8.9	0.02	0.3	0.03	0.3	0.05	0.6
	3	240	8.9	0.02	0.2	0.04	0.4	0.06	0.6

[a] Contains within-run, within-day, and between-day variance components.
[b] Contains within-run, within-day, between-day, and between-lot variance components.
[c] A single replicate outlier with a %HbA_{1c} value of 6.1 was removed from the analysis. The within-laboratory (total) %CV including the single replicate outlier was 2.4%.

For the ARCHITECT *c* 4000 System, the data in %HbA_{1c} (NGSP) are summarized in the following table.

Sample	Instrument	n	Mean %HbA_{1c}	Within-Run		Within-Laboratory Precision (Total)[a]		Precision with Additional Component of Between-Lot[b]	
				SD	%CV	SD	%CV	SD	%CV
Control 1	1	240	4.9	0.01	0.3	0.02	0.5	0.02	0.5
	2	240	4.9	0.01	0.3	0.03	0.7	0.03	0.7
	3	240	4.9	0.01	0.2	0.02	0.4	0.03	0.6
Control 2	1	240	9.6	0.02	0.2	0.03	0.3	0.03	0.3
	2	240	9.6	0.02	0.2	0.03	0.4	0.04	0.4
	3	240	9.6	0.02	0.2	0.03	0.3	0.04	0.4
Panel Near 4.0 %HbA_{1c}	1	240	4.4	0.01	0.2	0.02	0.5	0.04	0.9
	2	240	4.5	0.01	0.2	0.03	0.6	0.04	0.9
	3	240	4.4	0.01	0.2	0.02	0.4	0.04	1.0
Panel Range 6.0 - 7.0 %HbA_{1c}	1	240	6.5	0.01	0.2	0.02	0.3	0.05	0.7
	2	240	6.5	0.01	0.1	0.03	0.4	0.04	0.7
	3	240	6.5	0.01	0.2	0.02	0.3	0.05	0.8
Panel Range 8.0 - 10.0 %HbA_{1c}	1	240	9.0	0.01	0.1	0.03	0.3	0.06	0.6
	2	240	9.0	0.01	0.1	0.02	0.3	0.05	0.6
	3	240	9.0	0.01	0.2	0.03	0.3	0.06	0.6

[a] Contains within-run, within-day, and between-day variance components.
[b] Contains within-run, within-day, between-day, and between-lot variance components.

Method Comparison

The Hemoglobin A_{1c} assay is designed to have a slope of 1.00 ± 0.10 and a correlation coefficient (r) of ≥ 0.95 for specimens across the measuring interval when compared to an NGSP secondary reference laboratory method.

A correlation study was performed using CLSI protocol EP9-A2-IR[25] with Deming regression. Human whole blood specimen results from the Hemoglobin A_{1c} assay were compared with those from an NGSP secondary reference laboratory method.

For the ARCHITECT *c* 8000 and *c* 4000 Systems, the data in %HbA_{1c} are summarized in the following table.

	ARCHITECT vs. NGSP Secondary Reference Laboratory Method
N	128
Y - Intercept	-0.2
Correlation Coefficient	0.995
Slope	1.01
ARCHITECT Range (%HbA_{1c})	4.0 to 13.2 (ARCHITECT *c* 8000) 4.0 to 13.3 (ARCHITECT *c* 4000)
NGSP Secondary Reference Laboratory Range (%HbA_{1c})	4.0 to 13.4

Bias

IFCC

The Hemoglobin A_{1c} assay is designed to have a bias of ≤ 5% at 42.06, 47.53, and 53.00 mmol/mol HbA_{1c} using Deming regression.

NGSP

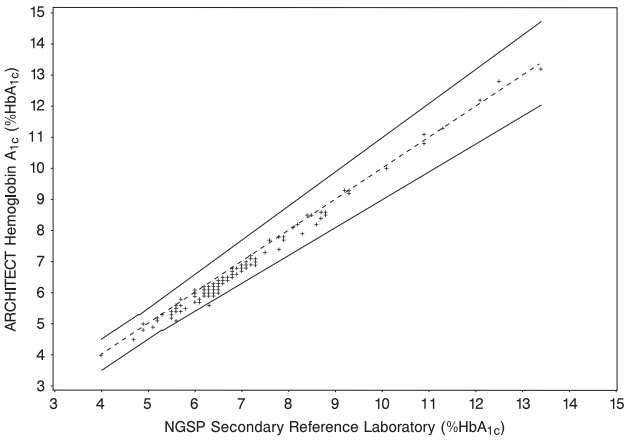
The Hemoglobin A_{1c} assay is designed to have a bias of ≤ 3% at 6.0, 6.5, and 7.0 %HbA_{1c} using Deming regression.

For the ARCHITECT *c* 8000 System, the bias in %HbA_{1c} (NGSP) ranged from -3.0% to -2.4%. For the ARCHITECT *c* 4000 System, the bias in %HbA_{1c} (NGSP) ranged from -2.3% to -1.8%.

Allowable Total Difference (ATD) Zone

The Hemoglobin A_{1c} assay is designed to have > 95% of observations in the ATD zone and the low limit of the two-sided 95% Confidence Interval (CI) > 89.5% using Deming regression.

For the ARCHITECT *c* 8000 System, the percentage of observations in the ATD zone was 99.2% (127/128) and the lower limit of the two-sided 95% CI was 95.7%. The ATD zone plot is presented below.



For the ARCHITECT *c* 4000 System, the percentage of observations in the ATD zone was 100.0% (128/128) and the lower limit of the two-sided 95% CI was 97.1%.

ARCHITECT *c* Systems Assay Parameters

HbA1c Whole Blood—Conventional and SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: **HbA1cWB** Type: **Photometric** Version: †
Number: **1106** Assay availability: **Enabled**
Run controls for onboard reagents by: **Lot**

● Reaction definition O Reagent / Sample O Validity checks

Reaction mode: **End up**

	Primary	Secondary	Read times
Wavelength:	**660** /	**804**	Main: **23 – 24**

Last required read: **24**
Absorbance range: **0.0000 – 3.0000** Color correction: ___ – ___
Sample blank type **Self** Blank : **15 – 16**

O Reaction definition ● Reagent / Sample O Validity checks

		R1	R2
Reagent: **A1C00**	Reagent volume:	**145**	**48**
Diluent: **A1cDIL**	Water volume:	___	___
Diluent dispense mode: **Type 0**	Dispense mode:	**Type 0**	**Type 0**

Dilution name	Sample	Diluted sample	Diluent	Water		Dilution factor	Default dilution
Std_WB:	**3.6**	**15.0**	**80**	___	=	**1:23.22**	●

O Reaction definition O Reagent / Sample ● Validity checks

Reaction check: **None**

Maximum absorbance variation: ___

Configure assay parameters — Calibration

O General ● Calibration O SmartWash O Results O Interpretation

Assay: **HbA1cWB** Assay number: **1106**
Calibration method: **Linear**

● Calibrators O Volumes O Intervals O Validity checks

Calibrator set: **HbA1c**
Replicates: **3** [Range 1 – 3]

Calibrator level:
Blank: **HbA1c1**
Cal 1: **HbA1c2**
Cal 2: **None**
Cal 3: **None**
Cal 4: **None**
Cal 5: **None**
Cal 6: **None**

Concentration: ♥
___††
††

O Calibrators ● Volumes O Intervals O Validity checks

Calibrator: **HbA1c**

Calibrator level	Sample	Diluted sample	Diluent	Water
Blank: **HbA1c1**	**15.0**	___	___	___
Cal 1: **HbA1c2**	**15.0**	___	___	___
Cal 2: **None**				
Cal 3: **None**				
Cal 4: **None**				
Cal 5: **None**				
Cal 6: **None**				

O Calibrators O Volumes ● Intervals O Validity checks

Calibration intervals:
Full interval: **1,200** (hours)
Calibration type:
Adjust type: **None**

O Calibrators O Volumes O Intervals ● Validity checks

Blank absorbance range: _____ – _____
Span: **Blank** – **Blank**
Span absorbance range: _____ – _____
Expected cal factor: **160.00**
Expected cal factor tolerance %: **99**

Configure assay parameters — SmartWash

O General O Calibration ● SmartWash O Results O Interpretation

Assay: **HbA1cWB**

COMPONENT	REAGENT / ASSAY	WASH	Volume	Replicates
R1	**AMIK9**	**Detergent A**	**345**	**1**
R1	**DIG00**	**Detergent A**	**345**	**1**
R1	**DGT0B**	**Detergent A**	**345**	**1**
R1	**GENT9**	**Detergent A**	**345**	**1**
R1	**TOBRA**	**Detergent A**	**345**	**1**
R1	**VANCO**	**Detergent A**	**345**	**1**
R1	**TP000**	**0.5% Acid Wash**	**345**	**1**
R2	**AMIK9**	**Detergent A**	**345**	**1**
R2	**DIG00**	**Detergent A**	**345**	**1**
R2	**DGT0B**	**Detergent A**	**345**	**1**
R2	**GENT9**	**Detergent A**	**345**	**1**
R2	**TOBRA**	**Detergent A**	**345**	**1**
R2	**VANCO**	**Detergent A**	**345**	**1**
Sample Probe*		**Water**		

* Sample Probe *Sample wash protocol* is **Maximum wash**.

HbA1c Whole Blood—Conventional and SI Units

Configure assay parameters — Results

O General O Calibration O SmartWash

Assay: **HbA1cWB**
Assay number: **1106**
Dilution default range: Result units: **umol/L**
Low-Linearity: **1.4308***
High-Linearity: **999999.9999****
Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units

Assay: **HbA1cWB**
Version: †
Result units: **umol/L**
Decimal places: **4** [Range 0-4]
Correlation factor: **1.0000**
Intercept: **0.0000**

Refer to **System Configuration, Configuration Screen** – **Assay Settings** in *Section 2* of the **ARCHITECT System Operations Manual** for additional information.

† Due to differences in instrument systems and unit configurations, version numbers may vary.

♥ Displays the number of decimal places defined in the decimal places parameter field.

†† Obtain value from Hemoglobin A1c Calibrator Value Sheet. **Important:** Value-assigned calibrator values are configured in the Calibrator set screen. It is also necessary to configure the Blank Concentration field in the assay parameter Calibration screen.

* Low-Linearity is the linear low value divided by the Standard dilution factor, then rounded up to the number of decimal places defined in the decimal places field.

** High-Linearity is set at the system maximum value. Since the Hemoglobin A1c is a ratio assay, the range of the assay is defined by the measuring interval.

ARCHITECT *c* Systems Assay Parameters

THb Whole Blood—Conventional and SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: **THbWB** Type: **Photometric** Version: †
Number: **1105** Assay availability: **Enabled**
Run controls for onboard reagents by: **Lot**

● Reaction definition O Reagent / Sample O Validity checks

Reaction mode: **End up**
Primary Secondary Read times
Wavelength: **476** / **804** Main: **15 – 16**
Last required read: **16**
Absorbance range: **0.0000 – 3.0000** Color correction: ___ – ___
Sample blank type: **None**

O Reaction definition ● Reagent / Sample‡ O Validity checks

		R1	R2
Reagent: **A1C00**	Reagent volume:	**0**	**0**
Diluent: <**None**>	Water volume:	___	___
Diluent dispense mode: **Type 0**	Dispense mode:	**Type 0**	**Type 0**

Dilution name	Sample	Diluted sample	Diluent	Water	Dilution factor	Default dilution
_____ :	___	___	___	___ =		●

‡ Error code 0247 occurs when navigating from this screen to another. Select OK. Confirm that the empty assay parameter fields align with this insert. DO NOT enter any value. Select Cancel to exit the screen.

O Reaction definition O Reagent / Sample ● Validity checks

Reaction check: **None**

Maximum absorbance variation: ___

Configure assay parameters — Calibration

O General ● Calibration O SmartWash O Results O Interpretation

Assay: **THbWB** Assay number: **1105**
Calibration method: **Linear**

● Calibrators O Volumes O Intervals O Validity checks

Calibrator set: **HbA1c**
Replicates: **3** [Range 1 – 3]

Calibrator level:
Blank: **HbA1c1**
Cal 1: **HbA1c2**
Cal 2: **None**
Cal 3: **None**
Cal 4: **None**
Cal 5: **None**
Cal 6: **None**

Concentration: ♥
___††
††

O Calibrators ● Volumes O Intervals O Validity checks

Calibrator: **HbA1c**

Calibrator level	Sample	Diluted sample	Diluent	Water
Blank: **HbA1c1**	**15.0**	___	___	___
Cal 1: **HbA1c2**	**15.0**	___	___	___
Cal 2: **None**				
Cal 3: **None**				
Cal 4: **None**				
Cal 5: **None**				
Cal 6: **None**				

O Calibrators O Volumes ● Intervals O Validity checks

Calibration intervals:
Full interval: **1,200** (hours)
Calibration type:
Adjust type: **None**

O Calibrators O Volumes O Intervals ● Validity checks

Blank absorbance range: _____ – _____
Span: **Blank** – **Blank**
Span absorbance range: _____ – _____
Expected cal factor: **433.00**
Expected cal factor tolerance %: **99**

Configure assay parameters — SmartWash

O General O Calibration ● SmartWash O Results O Interpretation

Assay: **THbWB**

COMPONENT	REAGENT / ASSAY	WASH	Volume	Replicates

THb Whole Blood—Conventional and SI Units

Configure assay parameters — Results

O General O Calibration O SmartWash

Assay: **THbWB**
Assay number: **1105**
Dilution default range: Result units: **umol/L**
Low-Linearity: **12.7302***
High-Linearity: **999999.9999****
Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units

Assay: **THbWB**
Version: †
Result units: **umol/L**
Decimal places: **4** [Range 0-4]
Correlation factor: **1.0000**
Intercept: **0.0000**

Refer to **System Configuration, Configuration Screen** – **Assay Settings** in *Section 2* of the **ARCHITECT System Operations Manual** for additional information.

† Due to differences in instrument systems and unit configurations, version numbers may vary.

♥ Displays the number of decimal places defined in the decimal places parameter field.

†† Obtain value from Hemoglobin A_{1c} Calibrator Value Sheet. **Important:** Value-assigned calibrator values are configured in the Calibrator set screen. It is also necessary to configure the Blank Concentration field in the assay parameter Calibration screen.

* Low-Linearity is the linear low value divided by the Standard dilution factor, then rounded up to the number of decimal places defined in the decimal places field.

** High-Linearity is set at the system maximum value. Since the Hemoglobin A_{1c} is a ratio assay, the range of the assay is defined by the measuring interval.

ARCHITECT *c* Systems Assay Parameters

Hb A1c Hemolysate—Conventional and SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: **Hb A1cH** Type: **Photometric** Version: †
Number: **1108** Assay availability: **Enabled**
Run controls for onboard reagents by: **Lot**

● Reaction definition O Reagent / Sample O Validity checks

Reaction mode: **End up**

	Primary	Secondary	Read times
Wavelength:	**660** /	**804**	Main: **23 – 24**

Last required read: **24**
Absorbance range: **0.0000 – 3.0000** Color correction: ___ – ___
Sample blank type: **Self** Blank: **15 – 16**

O Reaction definition ● Reagent / Sample O Validity checks

		R1	R2
Reagent:	**A1C00**	Reagent volume:	**145**	**48**
Diluent:	**<None>**	Water volume:	___	___
Diluent dispense mode:	**Type 0**	Dispense mode:	**Type 0**	**Type 0**

Dilution name	Sample	Diluted sample	Diluent	Water		Dilution factor	Default dilution
Std_H :	**15.0**	___	___	___	=	**1:1.00**	●

O Reaction definition O Reagent / Sample ● Validity checks

Reaction check: **None**

Maximum absorbance variation: ___

Configure assay parameters — Calibration

O General ● Calibration O SmartWash O Results O Interpretation

Assay: **Hb A1cH** Assay number: **1108**
Calibration method: **Linear**

● Calibrators O Volumes O Intervals O Validity checks

Calibrator set: **HbA1c**
Replicates: **3** [Range 1 – 3]

Calibrator level:		Concentration: ♥
Blank:	**HbA1c1**	___††
Cal 1:	**HbA1c2**	††
Cal 2:	**None**	
Cal 3:	**None**	
Cal 4:	**None**	
Cal 5:	**None**	
Cal 6:	**None**	

O Calibrators ● Volumes O Intervals O Validity checks

Calibrator: **HbA1c**

Calibrator level	Sample	Diluted sample	Diluent	Water
Blank: **HbA1c1**	**15.0**	___	___	___
Cal 1: **HbA1c2**	**15.0**	___	___	___
Cal 2: **None**				
Cal 3: **None**				
Cal 4: **None**				
Cal 5: **None**				
Cal 6: **None**				

O Calibrators O Volumes ● Intervals O Validity checks

Calibration intervals:
Full interval: **1,200** (hours)
Calibration type:
Adjust type: **None**

O Calibrators O Volumes O Intervals ● Validity checks

Blank absorbance range: _____ – _____
Span: **Blank** – **Blank**
Span absorbance range: _____ – _____
Expected cal factor: **160.00**
Expected cal factor tolerance %: **99**

Configure assay parameters — SmartWash

O General O Calibration ● SmartWash O Results O Interpretation

Assay: **HbA1cH**

COMPONENT	REAGENT / ASSAY	WASH	Volume	Replicates
R1	**AMIK9**	**Detergent A**	**345**	**1**
R1	**DIG00**	**Detergent A**	**345**	**1**
R1	**DGT0B**	**Detergent A**	**345**	**1**
R1	**GENT9**	**Detergent A**	**345**	**1**
R1	**TOBRA**	**Detergent A**	**345**	**1**
R1	**VANCO**	**Detergent A**	**345**	**1**
R1	**TP000**	**0.5% Acid Wash**	**345**	**1**
R2	**AMIK9**	**Detergent A**	**345**	**1**
R2	**DIG00**	**Detergent A**	**345**	**1**
R2	**DGT0B**	**Detergent A**	**345**	**1**
R2	**GENT9**	**Detergent A**	**345**	**1**
R2	**TOBRA**	**Detergent A**	**345**	**1**
R2	**VANCO**	**Detergent A**	**345**	**1**

HbA1c Hemolysate—Conventional and SI Units

Configure assay parameters — Results

O General O Calibration O SmartWash

Assay: **Hb A1cH**
Assay number: **1108**
Dilution default range: Result units: **umol/L**
Low-Linearity: **33.2230**
High-Linearity: **999999.9999****
Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units

Assay: **Hb A1cH**
Version: †
Result units: **umol/L**
Decimal places: **4** [Range 0-4]
Correlation factor: **23.2000**
Intercept: **0.0000**

Refer to **System Configuration, Configuration Screen – Assay Settings** in *Section 2* of the **ARCHITECT System Operations Manual** for additional information.

† Due to differences in instrument systems and unit configurations, version numbers may vary.
♥ Displays the number of decimal places defined in the decimal places parameter field.
†† Obtain value from Hemoglobin A1c Calibrator Value Sheet. **Important:** Value-assigned calibrator values are configured in the Calibrator set screen. It is also necessary to configure the Blank Concentration field in the assay parameter Calibration screen.
** High-Linearity is set at the system maximum value. Since the Hemoglobin A1c is a ratio assay, the range of the assay is defined by the measuring interval.

ARCHITECT *c* Systems Assay Parameters

THb Hemolysate—Conventional and SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: **THbH** Type: **Photometric** Version: †
Number: **1107** Assay availability: **Enabled**
Run controls for onboard reagents by: **Lot**

● Reaction definition O Reagent / Sample O Validity checks

Reaction mode: **End up**
Primary / Secondary — Read times
Wavelength: **476** / **804** Main: **15 – 16**
Last required read: **16**
Absorbance range: **0.0000 – 3.0000** Color correction: ___ – ___
Sample blank type: **None**

O Reaction definition ● Reagent / Sample‡ O Validity checks

		R1	R2
Reagent: **A1C00**	Reagent volume:	**0**	**0**
Diluent: **<None>**	Water volume:	___	___
Diluent dispense mode: **Type 0**	Dispense mode:	**Type 0**	**Type 0**

Dilution name	Sample	Diluted sample	Diluent	Water		Dilution factor	Default dilution
_____ :	___	___	___	___	=		●

‡ Error code 0247 occurs when navigating from this screen to another. Select OK. Confirm that the empty assay parameter fields align with this insert. DO NOT enter any value. Select Cancel to exit the screen.

O Reaction definition O Reagent / Sample ● Validity checks

Reaction check: **None**

Maximum absorbance variation: ___

Configure assay parameters — Calibration

O General ● Calibration O SmartWash O Results O Interpretation

Assay: **THbH** Assay number: **1107**
Calibration method: **Linear**

● Calibrators O Volumes O Intervals O Validity checks

Calibrator set: **HbA1c**
Replicates: **3** [Range 1 – 3]

Calibrator level:
Blank: **HbA1c1**
Cal 1: **HbA1c2**
Cal 2: **None**
Cal 3: **None**
Cal 4: **None**
Cal 5: **None**
Cal 6: **None**

Concentration: ♥
___††
††

O Calibrators ● Volumes O Intervals O Validity checks

Calibrator: **HbA1c**

Calibrator level	Sample	Diluted sample	Diluent	Water
Blank: **HbA1c1**	**15.0**	___	___	___
Cal 1: **HbA1c2**	**15.0**	___	___	___
Cal 2: **None**				
Cal 3: **None**				
Cal 4: **None**				
Cal 5: **None**				
Cal 6: **None**				

O Calibrators O Volumes ● Intervals O Validity checks

Calibration intervals:
Full interval: **1,200** (hours)
Calibration type:
Adjust type: **None**

O Calibrators O Volumes O Intervals ● Validity checks

Blank absorbance range: _____ – _____
Span: **Blank** – **Blank**
Span absorbance range: _____ – _____
Expected cal factor: **433.00**
Expected cal factor tolerance %: **99**

Configure assay parameters — SmartWash

O General O Calibration ● SmartWash O Results O Interpretation

Assay: **THbH**

COMPONENT	REAGENT / ASSAY	WASH	Volume	Replicates

ThB Hemolysate—Conventional and SI Units

Configure assay parameters — Results

O General O Calibration O SmartWash

Assay: **THbH**
Assay number: **1107**
Dilution default range: Result units: **umol/L**
Low-Linearity: **295.5947**
High-Linearity: **999999.9999****
Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units

Assay: **THbH**
Version: †

Result units: **umol/L**
Decimal places: **4** [Range 0-4]

Correlation factor: **23.2000**
Intercept: **0.0000**

Refer to **System Configuration, Configuration Screen** – **Assay Settings** in *Section 2* of the **ARCHITECT System Operations Manual** for additional information.

† Due to differences in instrument systems and unit configurations, version numbers may vary.
♥ Displays the number of decimal places defined in the decimal places parameter field.
†† Obtain value from Hemoglobin A_{1c} Calibrator Value Sheet. **Important:** Value-assigned calibrator values are configured in the Calibrator set screen. It is also necessary to configure the Blank Concentration field in the assay parameter Calibration screen.
** High-Linearity is set at the system maximum value. Since the Hemoglobin A_{1c} is a ratio assay, the range of the assay is defined by the measuring interval.

ARCHITECT *c* Systems Assay Parameters

Percent A_{1c} Whole Blood (NGSP)—Conventional Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: %A1cWB Type: Calculated
Number: 3075 Assay Availability: Enabled

Formula: (ASSAY1/ASSAY2) * 1000 * 0.09148 + 2.152

Selected assays:

	Minimum	Maximum
ASSAY1:	HbA1cWB	
	___	___
ASSAY2:	THbWB	
	___	___

Configure assay parameters — Results

O General O Calibration O SmartWash ● Results O Interpretation

Assay: %A1cWB
Assay number: 3075
Result units: %

Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units — Assay Settings

Assay: %A1cWB
Version: †
Result units: %
Decimal places: 1 {Range 0 - 4}

A_{1c} Whole Blood (IFCC)—SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: A1cWB Type: Calculated
Number: 3074 Assay Availability: Enabled

Formula: (ASSAY1/ASSAY2) * 1000

Selected assays:

	Minimum	Maximum
ASSAY1:	HbA1cWB	
	___	___
ASSAY2:	THbWB	
	___	___

Configure assay parameters — Results

O General O Calibration O SmartWash ● Results O Interpretation

Assay: A1cWB
Assay number: 3074
Result units: mM/mol

Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units — Assay Settings

Assay: A1cWB
Version: †
Result units: mM/mol
Decimal places: 2 {Range 0 - 4}

Percent A_{1c} Hemolysate (NGSP)—Conventional Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: %A1cH Type: Calculated
Number: 3077 Assay Availability: Enabled

Formula: (ASSAY1/ASSAY2) * 1000 * 0.09148 + 2.152

Selected assays:

	Minimum	Maximum
ASSAY1:	HbA1cH	
	___	___
ASSAY2:	THbH	
	___	___

Configure assay parameters — Results

O General O Calibration O SmartWash ● Results O Interpretation

Assay: %A1cH
Assay number: 3077
Result units: %

Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units — Assay Settings

Assay: %A1cH
Version: †
Result units: %
Decimal places: 1 {Range 0 - 4}

A_{1c} Hemolysate (IFCC)—SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: A1cH Type: Calculated
Number: 3076 Assay Availability: Enabled

Formula: (ASSAY1/ASSAY2) * 1000

Selected assays:

	Minimum	Maximum
ASSAY1:	HbA1cH	
	___	___
ASSAY2:	THbH	
	___	___

Configure assay parameters — Results

O General O Calibration O SmartWash ● Results O Interpretation

Assay: A1cH
Assay number: 3076
Result units: mM/mol

Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME

Configure result units — Assay Settings

Assay: A1cH
Version: †
Result units: mM/mol
Decimal places: 2 {Range 0 - 4}

Refer to **Assay Configuration** in *Section 2* of the **ARCHITECT System Operations Manual** for additional information.
† Due to differences in instrument systems and unit configurations, version numbers may vary.

BIBLIOGRAPHY

1. Bry L, Chen PC, Sacks DB. Effects of hemoglobin variants and chemically modified derivatives on assays for glycohemoglobin. *Clin Chem* 2001;47(2):153–163.
2. Sacks DB. The diagnosis of diabetes is changing: How implementation of hemoglobin A1c will impact clinical laboratories. *Clin Chem* 2009;55(9): 1612–1614.
3. American Diabetes Association Workgroup Report: International Expert Committee report on the role of the A1c assay in the diagnosis of diabetes. *Diabetes Care* 2009;32(7):1327–1334.
4. Fonseca V, Inzucchi SE, Ferrannini E. Redefining the diagnosis of diabetes using glycated hemoglobin. *Diabetes Care* 2009;32(7):1344–1345.
5. American Diabetes Association Executive Summary: Standards of medical care in diabetes - 2010. *Diabetes Care* 2010;33(Suppl 1):S4–S10.
6. Sacks DB, Bruns DE, Goldstein DE, et al. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem* 2002;48(3):436–472.
7. American Diabetes Association. Position Statement: Standards of medical care in diabetes - 2012. *Diabetes Care* 2012;35(Suppl 1):S11–S63.
8. Rochman H. Hemoglobin A1c and diabetes mellitus. *Ann Clin Lab Sci* 1980;10(2):111–115.
9. 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* 1993;329(14):977–986.
10. Larsen ML, Hørder M, Mogensen EF. Effect of long-term monitoring of glycosylated hemoglobin levels in insulin-dependent diabetes mellitus. *N Engl J Med* 1990;323(15):1021–1025.
11. 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.
12. US Department of Labor, Occupational Safety and Health Administration, 29 CFR Part 1910.1030, Bloodborne pathogens.
13. US Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories*, 5th ed. Washington, DC: US Government Printing Office, December 2009.
14. World Health Organization. *Laboratory Biosafety Manual.* 3rd ed. Geneva: World Health Organization; 2004.
15. Clinical and Laboratory Standards Institute (CLSI). *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition.* CLSI Document M29-A4. Wayne, PA: CLSI; 2014.
16. Goldstein DE, Wiedmeyer HM, England JD, et al. Recent advances in glycosylated hemoglobin measurements. *Crit Rev Clin Lab Sci* 1984;21(3): 187–228.
17. Peacock I. Glycosylated haemoglobin: measurement and clinical use. *J Clin Pathol* 1984;37:841–851.
18. Horton BF, Huisman TH. Studies on the heterogeneity of haemoglobin, VII. Minor haemoglobin components in haematological diseases. *Br J Haematol* 1965;11(3):296–304.
19. Lind T, Cheyne GA. Effect of normal pregnancy upon the glycosylated haemoglobins. *Br J Obstet Gynaecol* 1979;86(3):210–213.
20. American Diabetes Association. Position Statement: Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2010;33(Suppl 1):S62–S69.
21. National Committee for Clinical Laboratory Standards (NCCLS). *Protocols for Determination of Limits of Detection and Limits of Quantitation: Approved Guideline.* NCCLS Document EP17-A. Wayne, PA: NCCLS; 2004.
22. National Committee for Clinical Laboratory Standards (NCCLS). *Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.* NCCLS Document EP6-A. Wayne, PA: NCCLS; 2003.
23. Clinical and Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition.* CLSI Document EP07-A2. Wayne, PA: CLSI; 2005.
24. National Committee for Clinical Laboratory Standards (NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition.* NCCLS Document EP5-A2. Wayne, PA: NCCLS; 2004.
25. Clinical and Laboratory Standards Institute (CLSI). *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Second Edition (Interim Revision).* CLSI Document EP9-A2-IR. Wayne, PA: CLSI; 2010.

TRADEMARKS

Key to Symbols

ISO 15223 Symbols	
	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
IVD	*In Vitro* Diagnostic Medical Device
LOT	Batch code/Lot number
REF	Catalog number/List number
SN	Serial number

Other Symbols	
A1cDIL	Hemoglobin A1c Diluent
CONTAINS: AZIDE	Contains sodium azide. Contact with acids liberates very toxic gas.
DISTRIBUTED IN THE USA BY	Distributed in the USA by
FOR USE WITH	Identifies products to be used together
INFORMATION FOR USA ONLY	Information needed for United States of America only
MANUFACTURED FOR	Manufactured for
PRODUCT OF CANADA	Product of Canada
R1	Reagent 1
R2	Reagent 2
Rx ONLY	For use by or on the order of a physician only (applicable to USA classification only)

Customer Service: Contact your local representative or find country-specific contact information on www.corelaboratory.abbott.

Abbott GmbH
Max-Planck-Ring 2
65205 Wiesbaden
Germany
+49-6122-580

MANUFACTURED FOR
Abbott Laboratories

DISTRIBUTED IN THE USA BY
Abbott Laboratories
Abbott Park, IL 60064 USA

Revised May 2022

Abbott