

Apolipoprotein B (APO B)

Current Revision and Date ^a	Rev. 02, 2019-05
Product Name	Atellica CH Apolipoprotein B (APO B) REF 11097626 (300 tests)
Abbreviated Product Name	Atellica CH APO B
Test Name/ID	APO B
Systems	Atellica CH Analyzer
Materials Required but Not Provided	Atellica CH APO A1 & B CAL REF 11099329
Specimen Types	Serum and plasma (lithium heparin)
Sample Volume	5 µL
Measuring Interval	15–200 mg/dL (0.15–2.00 g/L)

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



Intended Use

The Atellica® CH Apolipoprotein B (APO B) assay is for *in vitro* diagnostic use in the quantitative determination of apolipoprotein B in human serum and plasma (lithium heparin) using the Atellica® CH Analyzer. Such measurements are used to aid in the assessment of risk for arteriosclerosis and coronary artery disease.

Summary and Explanation¹⁻⁴

Apolipoprotein B (APO B) is a distinct, lipid-binding protein that is the major protein moiety of all lipoproteins other than high-density lipoprotein (HDL).¹⁻³ APO B is essential to the formation and release of lipoproteins into the plasma and interacts with the LDL receptors of peripheral cells thereby functioning in the recognition of cellular receptors for the catabolism of LDL.^{2,3}

Studies show a correlation between the development of coronary atherosclerosis and abnormal concentrations of lipoproteins. In atherosclerosis, the inner layer of the arterial wall thickens due to the accumulation of cellular material and deposits of several substances, particularly lipids.³ Because apolipoproteins are unique markers for the identification and differentiation of lipoproteins, they are the most probable determinants of the structural integrity and functional specificity of lipoproteins.³ Measurement of APO B in serum of patients with significant arteriosclerotic alterations shows APO B levels significantly higher than a normal patient population.⁴ Abnormal APO B values also occur with dyslipoproteinemias. Adult-onset diabetes and liver diseases including acute hepatitis and fatty liver result in elevated APO B values.¹

Numerous studies suggest that serum apolipoprotein A-1 (APO A-1) and APO B levels indicate the severity and extent of coronary artery stenosis better than serum total cholesterol and triglyceride.² In addition, studies indicate that patients with atherosclerosis are better distinguished from patients without the disease by the finding of increased plasma APO B levels than by the findings of decreased HDL-C and increased LDL-C levels.³ Measuring both APO A-1 and APO B and expressing the data as a ratio has been shown to be more effective than APO A-1 or APO B alone.²

Principles of the Procedure

The Atellica CH APO B assay is a polyethylene glycol (PEG) enhanced immunoturbidimetric assay. A sample containing human apolipoprotein B and specific antiserum form an insoluble complex that is measured turbidimetrically at 340/694 nm. By constructing a standard curve from the absorbances of standards, the concentration of apolipoprotein B is determined.

Reagents

Material Description	Storage	Stability ^a
Atellica CH APO B	Unopened at 2–8°C	Until expiration date on product
Pack 1 (P1)	Onboard per well	30 days
Well 1 (W1) Reagent 1 (R1) 10 mL Polyethylene glycol (4%); sodium azide (0.09%)		
Well 2 (W2) Reagent 1 (R1) 10 mL Polyethylene glycol (4%); sodium azide (0.09%)		
Pack 2 (P2)		
Well 1 (W1) Reagent 2 (R2) 4.1 mL Antihuman APO B (goat); sodium azide (0.09%)		
Well 2 (W2) Reagent 2 (R2) 4.1 mL Antihuman APO B (goat); sodium azide (0.09%)		

^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](https://www.siemens.com/healthineers).

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

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

Unopened reagents are stable until the expiration date on the product when stored at 2–8°C.

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

Onboard Stability

Reagents are stable onboard the system for 30 days per well. 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 serum and plasma (lithium heparin) are the recommended sample types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.⁵
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.⁶
- Follow the instructions provided with your specimen collection device for use and processing.⁷
- Allow blood specimens to clot completely before centrifugation.⁸
- Keep tubes capped at all times.⁸

Storing the Specimen

Specimens may be stored for up to 7 days at 2–8°C or stored frozen for up to 3 months at -20°C.⁹

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 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.
- Fibrin or other particulate matter.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.⁸

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
11097626	Pack 1 (P1) Well 1 (W1) 10.0 mL of Atellica CH APO B Reagent 1 Well 2 (W2) 10.0 mL of Atellica CH APO B Reagent 1 Pack 2 (P2) Well 1 (W1) 4.1 mL of Atellica CH APO B Reagent 2 Well 2 (W2) 4.1 mL of Atellica CH APO B Reagent 2	2 x 150

Materials Required but Not Provided

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

REF	Description
	Atellica CH Analyzer ^a
11099329	Atellica CH APO A1 & B CAL (calibrator) 5 x 1.0 mL calibrator CAL 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.

Assay Procedure

The system automatically performs the following steps:

1. For serum/plasma, dispenses 11 µL of primary sample and 224.4 µL of Atellica CH Diluent into a dilution cuvette.
2. Dispenses 83 µL of Reagent 1 into a reaction cuvette.
3. Dispenses 5 µL of pre-diluted sample into a reaction cuvette.

4. Measures the absorbance after sample addition.
5. Dispenses 17 µL of Reagent 2 into a reaction cuvette.
6. Mixes and incubates the mixture at 37°C.
7. Measures the absorbance after Reagent 2 addition.
8. 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 APO B assay, use Atellica CH APO A1 & B CAL. Use the calibrators in accordance with the calibrator instructions for use.

Note The reconstituted calibrator requires a 1:4 manual dilution prior to use, per 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	60
Pack Calibration	30
Reagent Onboard Stability	30

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 APO B 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 system determines the result using the calculation scheme described in the online help. The system reports results in mg/dL (common units) or g/L (SI units), depending on the units defined when setting up the assay.

Conversion formula: $\text{mg/dL} \times 0.01 = \text{g/L}$

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

The Atellica CH APO B assay is limited to the detection of apolipoprotein B in human serum and plasma (lithium heparin).

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.¹⁰

According to published studies such as Clinical Guide to Laboratory Test, 3rd edition, by NW Tietz and *Lipoprotein Cholesterol, and Apoprotein Distribution in Selected US Communities* by SA Brown, et al. expected values vary according to age, sex, and race.

Group	Specimen Type	Reference Interval mg/dL (g/L)
Males	Serum/plasma ^{11,12}	46–174 (0.46–1.74)
Females	Serum/plasma ^{11,12}	46–142 (0.46–1.42)

The above APO B reference ranges, which represent ranges seen in selected U.S. populations, should be used as a rough guide in evaluating the degree of abnormality.¹¹

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.¹⁰

Performance Characteristics

Measuring Interval

The Atellica CH APO B assay provides results from 15 mg/dL (0.15 g/L) to 200 mg/dL (2.00 g/L). The system flags all values that are outside the specified measuring interval.

Extended Measuring Interval

An automatic repeat condition for this assay extends the measuring interval to 400 mg/dL (4.00 g/L) for serum and plasma. You may configure the system to trigger an automatic repeat. Automatic repeat results will be flagged **Autorepeat**.

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) $\leq$ limit of detection (LoD) and LoD $\leq$ 15 mg/dL ($\leq$ 0.15 g/L).

The LoD corresponds to the lowest concentration of apolipoprotein B that can be detected with a probability of 95%. The LoD for the Atellica CH APO B assay is 2 mg/dL (0.02 g/L), and was determined using 120 determinations, with 60 blank and 60 low level replicates, and a LoB of 1 mg/dL (0.01 g/L).

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

Precision

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 ($N \geq 80$ for each sample). The following results were obtained:

Sample Type	N	Mean mg/dL (g/L)	Repeatability		Designed to be $\leq$		Within-Lab Precision		Designed to be $\leq$
			SD ^a mg/dL (g/L)	CV ^b (%)	CV (%)		SD mg/dL (g/L)	CV (%)	CV (%)
Plasma	80	61 (0.61)	1.0 (0.010)	1.6	5.0		3.7 (0.037)	6.1	7.0
Serum	80	120 (1.20)	1.1 (0.011)	0.9	5.0		4.2 (0.042)	3.5	7.0
QC	80	158 (1.58)	0.9 (0.009)	0.6	5.0		4.4 (0.044)	2.8	7.0

^a Standard deviation.

^b Coefficient of variation.

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

Assay Comparison

The Atellica CH APO B assay is designed to have a correlation coefficient of > 0.950 and a slope of 1.0 ± 0.10 compared to ADVIA® Chemistry 1800 APO B. Assay comparison was determined using the weighted Deming linear regression model in accordance with CLSI Document EP09-A3.¹⁵ The following results were obtained:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N ^a	r ^b
Serum	ADVIA Chemistry 1800 APO B	$y = 0.99x - 4 \text{ mg/dL}$ ($y = 0.99x - 0.04 \text{ g/L}$)	29–204 mg/dL (0.29–2.04 g/L)	113	0.999

^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.

Specimen Equivalency

Specimen equivalency was determined using the Deming linear regression model in accordance with CLSI Document EP09-A3.¹⁵ The following results were obtained:

Specimen (y)	Reference Specimen (x)	Regression Equation	Sample Interval	N ^a	r ^b
Lithium heparin plasma	Serum	$y = 0.97x + 0 \text{ mg/dL}$ ($y = 0.97x + 0.00 \text{ g/L}$)	19–182 mg/dL (0.19–1.82 g/L)	50	0.993

^a Number of samples tested.

^b Correlation coefficient.

Agreement of the specimen types may vary depending on the study design and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Hemolysis, Icterus, and Lipemia (HIL)

The Atellica CH APO B assay is designed to have $\leq 10\%$ interference from hemoglobin, bilirubin, and lipemia. Interfering substances at the levels indicated in the table below were tested in serum in accordance with CLSI Document EP07-A2 using the Atellica CH APO B 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 $> 10\%$ is considered interference. Analyte results should not be corrected based on this bias.

Substance	Substance Test Concentration Common Units (SI Units)	Analyte Concentration mg/dL (g/L)	Percent Bias
Hemoglobin	525 mg/dL (0.325 mmol/L)	40 (0.40)	-5
	525 mg/dL (0.325 mmol/L)	139 (1.39)	-2
Bilirubin, conjugated	30 mg/dL (513 $\mu\text{mol/L}$)	38 (0.38)	-3
	30 mg/dL (513 $\mu\text{mol/L}$)	128 (1.28)	-2
Bilirubin, unconjugated	30 mg/dL (513 $\mu\text{mol/L}$)	40 (0.40)	-3
	30 mg/dL (513 $\mu\text{mol/L}$)	136 (1.36)	1
Lipemia (Intralipid®)	650 mg/dL (7.35 mmol/L)	41 (0.41)	0
	650 mg/dL (7.35 mmol/L)	135 (1.35)	0

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

High-Dose Hook Effect

High APO B levels can cause a paradoxical decrease in signal as a result of the high-dose hook effect. In the Atellica CH APO B assay, APO B levels as high as 5600 mg/dL (56.00 g/L) will read > 200 mg/dL (2.00 g/L).

Standardization

The Atellica CH APO B assay is traceable to the World Health Organization-International Federation of Clinical Chemistry and Laboratory Medicine (WHO-IFCC) reference material SP3-07.

Assigned values for calibrators are traceable to this standardization.¹⁷

Technical Assistance

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

siemens.com/healthineers

References

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9. Wu AHB. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. St. Louis, MO: Saunders; 2006:146.
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11. Tietz NW. *Clinical Guide to Laboratory Tests*. 3rd ed. Philadelphia, PA: WB Saunders Company; 1995:68-71.
12. Brown SA, Hutchinson R, Morrisett J, et al. Plasma lipid, lipoprotein cholesterol, and apoprotein distributions in selected US communities. *Arterioscler Thromb.* 1993;13(8):1139-1158.

13. Clinical and Laboratory Standards Institute. *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2012. CLSI Document EP17-A2.
14. Clinical and Laboratory Standards Institute. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document EP05-A3.
15. Clinical and Laboratory Standards Institute. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013. CLSI Document EP09-A3.
16. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document EP07-A2.
17. Data on file at Siemens Healthcare Diagnostics.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
 Rev. 01	Version of instructions for use
 siemens.com/healthcare	Internet URL address to access the electronic instructions for use
 siemens.com/document-library	
Rev. 	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.
	Corrosive
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable

Symbol	Symbol Title and Description
	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
	<i>In vitro</i> 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.
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

Symbol	Symbol Title and Description
	Authorized Representative in the European Community
	Use-by date Use by the designated date.
	Batch code
	Catalog number
	Recycle
	Printed with soy ink
	CE Mark
	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year-month-day)
	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
	Common Units
	International System of Units
	Material
	Unique material identification number
	Name of control
	Type of control

Legal Information

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