SIEMENS Healthineers

Total Iron Binding Capacity (TIBC)

Current Revision and Date[a]	Rev. 02, 2019-11	
Product Name	Atellica CH Total Iron Binding Capacity (TIBC)	REF 11097525 (800 tests)
Abbreviated Product Name	Atellica CH TIBC	
Test Name/ID	TIBC	
Systems	Atellica CH Analyzer	
Materials Required but Not Provided	Atellica CH SPCL CHEM CAL	REF 11099438
Specimen Types	Serum	
Sample Volume	24 µL	
Measuring Interval	40–670 µg/dL (7.16–119.93 µmol/L)	

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

CE

Intended Use

The Atellica® CH Total Iron Binding Capacity (TIBC) assay is for *in vitro* diagnostic use in the quantitative measurement of total iron binding capacity in human serum on the Atellica® CH Analyzer. Measurement of total iron binding capacity is used in the diagnosis and treatment of anemia.[1-4]

Summary and Explanation

This assay measures total iron binding capacity in a sequential process that is monitored spectrophotometrically. The sample is added to an acidic Reagent 1 (R1) containing iron and an iron binding dye. Bound iron is released by the acidic R1. Neutral Reagent 2 (R2) buffer is added and the shift in pH allows iron to bind and saturate the transferrin from the sample. The decrease in absorbance is directly proportional to the iron binding capacity of the serum sample.

Principles of the Procedure

The Atellica CH Total Iron Binding Capacity (TIBC) assay uses two reagents in a sequential process that is monitored spectrophotometrically.

Step 1

1. The system adds R1, an acidic buffer containing an iron-binding dye (Chromazurol B) and ferric chloride, to the serum sample.
2. The low pH of R1 releases iron from transferrin.
3. The iron forms a colored complex with the dye at the end of this first step. The colored complex represents both the serum iron and excess iron already present in R1.

Step 2

1. The system then adds R2, a neutral buffer.
2. The pH shifts, resulting in a large increase in affinity of transferrin for iron.
3. The serum transferrin rapidly binds the iron by abstracting it from the dye-iron complex.
4. The observed decrease in absorbance of the colored dye-iron complex is directly proportional to the total iron-binding capacity of the serum sample.

Reaction Equation

$$Fe^{3+} + \text{Chromazurol B} + Fe^{-}\ \text{Transferrin} \xrightarrow{H^{+}} Fe^{-}\ \text{Chromazurol B} + \text{Transferrin}$$

$$Fe^{-}\ \text{Chromazurol B} + \text{Transferrin} \xrightarrow{\text{Neutral pH}} Fe^{-}\ \text{Transferrin} + Fe^{-}\ \text{Chromazurol B}$$

Reagents

Material Description	Storage	Stability[a]
Atellica CH TIBC	Unopened at 2–8°C	Until expiration date on product
Pack 1 (P1)	Onboard per well	7 days
Well 1 (W1) Reagent 1 (R1) 9.2 mL Chromazurol B (166 µmol/L); cetrimide (735 µmol/L); ferric chloride (16 µmol/L); acetate buffer; stabilizers; preservatives		
Well 2 (W2) Reagent 1 (R1) 9.2 mL Chromazurol B (166 µmol/L); cetrimide (735 µmol/L); ferric chloride (16 µmol/L); acetate buffer; stabilizers; preservatives		
Pack 2 (P2)		
Well 1 (W1) Reagent 2 (R2) 5.5 mL Sodium bicarbonate buffer (338 mmol/L); stabilizers; preservatives		
Well 2 (W2) Reagent 2 (R2) 5.5 mL Sodium bicarbonate buffer (338 mmol/L); stabilizers; preservatives		

[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.

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.

H317 **P280, P272, P302+P352, 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:** reaction mass of: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1) (R1 and R2)

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 7 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

Serum is the recommended sample type 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

Separated specimens may be stored for up to 4 days at room temperature or for up to 7 days at 2–8°C or stored frozen for up to 2 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 24 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
11097525	**Pack 1 (P1)** Well 1 (W1) 9.2 mL of Atellica CH TIBC Reagent 1 Well 2 (W2) 9.2 mL of Atellica CH TIBC Reagent 1 **Pack 2 (P2)** Well 1 (W1) 5.5 mL of Atellica CH TIBC Reagent 2 Well 2 (W2) 5.5 mL of Atellica CH TIBC Reagent 2	4 x 200

Materials Required but Not Provided

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

REF	Description	
	Atellica CH Analyzer[a]	
11099438	Atellica CH SPCL CHEM CAL (calibrator)	10 x 5.0 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, dispenses 50 µL of primary sample and 200 µL of Atellica CH Diluent into a dilution cuvette.
2. Dispenses 60 µL of Reagent 1 into a reaction cuvette.
3. Dispenses 24 µL of pre-diluted sample into a reaction cuvette.
4. Measures the absorbance after sample addition.
5. Dispenses 24 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 TIBC assay, use Atellica CH SPCL CHEM 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	7
Reagent Onboard Stability	7

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 TIBC 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 µg/dL (common units) or µmol/L (SI units), depending on the units defined when setting up the assay.

Conversion formula: µg/dL x 0.179 = µmol/L

Use the following formula to obtain serum UIBC from serum TIBC and iron: TIBC - Iron = UIBC (µg/dL or µmol/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 TIBC assay is limited to the detection of total iron binding capacity in human serum.

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]

The reference interval for total iron binding capacity is 250–425 µg/dL (44.75–76.08 µmol/L) for adults.[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 TIBC assay provides results from 40–670 µg/dL (7.16–119.93 µmol/L). The system flags all values that are outside the specified measuring interval.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[12] The assay is designed to have a limit of blank (LoB) < limit of detection (LoD) and LoD ≤ 40 µg/dL (7.16 µmol/L).

The LoD corresponds to the lowest concentration of total iron binding capacity that can be detected with a probability of 95%. The LoD for the Atellica CH TIBC assay is 9 µg/dL (1.61 µmol/L), and was determined using 120 determinations, with 60 blank and 60 low level replicates, and a LoB of 6 µg/dL (1.07 µmol/L).

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

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[13] Samples were assayed on an Atellica CH Analyzer in duplicate in 2 runs per day for 20 days (N ≥ 80 for each sample). The following results were obtained:

			Repeatability		Designed to be ≤	Within-Lab Precision		Designed to be ≤
Sample Type	N	Mean µg/dL (µmol/L)	SD[a] µg/dL (µmol/L)	CV[b] (%)	CV (%)	SD µg/dL (µmol/L)	CV (%)	CV (%)
Serum QC	80	222 (39.74)	1.72 (0.31)	0.8	5.0	2.91 (0.52)	1.3	7.0
Serum	80	370 (66.23)	1.54 (0.28)	0.4	5.0	2.63 (0.47)	0.7	7.0
Serum	80	536 (95.94)	2.05 (0.37)	0.4	5.0	3.16 (0.57)	0.6	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 TIBC assay is designed to have a correlation coefficient of > 0.950 and a slope of 1.0 ± 0.10 compared to ADVIA® Chemistry 1800 TIBC. Assay comparison was determined using the Weighted Deming linear regression model in accordance with CLSI Document EP09-A3.[14] The following results were obtained:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ADVIA Chemistry 1800 TIBC	y = 1.05x - 20 µg/dL (y = 1.05x - 3.58 µmol/L)	132–596 µg/dL (23.63–106.68 µmol/L)	137	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.

Interferences

Hemolysis, Icterus, and Lipemia (HIL)

The Atellica CH TIBC assay is designed to have ≤ 10% 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 TIBC assay.[15]

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 µg/dL (µmol/L)	Percent Bias
Hemoglobin	1000 mg/dL (0.624 mmol/L) 1000 mg/dL (0.624 mmol/L)	413 (73.93) 631 (112.95)	-1 -3
Bilirubin, conjugated	25 mg/dL (428 µmol/L) 19 mg/dL (325 µmol/L)	428 (76.61) 628 (112.41)	-3 -1
Bilirubin, unconjugated	25 mg/dL (428 µmol/L) 25 mg/dL (428 µmol/L)	428 (76.61) 587 (105.07)	-1 -5
Lipemia (Intralipid®)	375 mg/dL (4.2 mmol/L) 250 mg/dL (2.8 mmol/L)	430 (76.97) 608 (108.83)	10 10
Lipemia (Triglycerides)	1000 mg/dL (11.3 mmol/L) 500 mg/dL (5.7 mmol/L)	412 (73.75) 627 (112.23)	7 9

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

Standardization

The Atellica CH TIBC assay is traceable to an internal standard.

Assigned values for calibrators are traceable to this standardization.[16]

Technical Assistance

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

siemens.com/healthineers

References

1. Burtis CA, Ashwood ER. *Tietz Fundamentals of Clinical Chemistry*. 5th ed. Philadelphia, PA: WB Saunders Company; 2001:992.
2. Clinical and Laboratory Standards Institute (formerly NCCLS). *Determination of Serum Iron and Total Iron Binding Capacity and Percent Transferrin Saturation; Approved Standard*. NCCLS Document H17-A. Wayne, PA: Clinical and Laboratory Standards Institute; 1998.
3. Starr RT. Use of an alumina column in estimating total iron-binding capacity. *Clin Chem*. 1980;26(1):156–158.
4. Gambino R, Desvarieux E, Orth M. The relation between chemically measured total iron-binding capacity concentrations and immunologically measured transferrin concentrations in human serum. *Clin Chem*. 1997;43:2408–2412.
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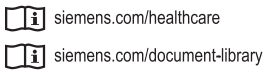
6. Clinical and Laboratory Standards Institute. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2007. CLSI Document GP41-A6.
7. Clinical and Laboratory Standards Institute. *Tubes and Additives for Venous and Capillary Blood Specimen Collection; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP39-A6.
8. Clinical and Laboratory Standards Institute. *Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP44-A4.
9. Young DS. *Effects of Preanalytical Variables on Clinical Laboratory Tests*. 3rd ed. Washington, DC: AACC Press; 2007:570.
10. Clinical and Laboratory Standards Institute. *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document EP28-A3c.
11. Burtis CA, Ashwood ER. *Tietz Fundamentals of Clinical Chemistry*. 5th ed. WB Saunders Company; 2001:992.
12. 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.
13. 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.
14. 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.
15. 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.
16. 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
	Version of instructions for use
	Internet URL address to access the electronic instructions for use
	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
	Oxidizing
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.

Symbol	Symbol Title and Description
	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.
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
	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

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

Legal Information

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