Alinity c UIBC-22

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BIENNIAL REVIEW:

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SUPERSEDES: Procedure titled _____

INTENDED USE

The Alinity c UIBC assay is used for the quantitative determination of unsaturated iron-binding capacity (UIBC) in serum or plasma on the Alinity c analyzer.

SUMMARY AND EXPLANATION OF THE TEST

Iron status is used in the diagnosis and management of some hematologic and hepatic conditions. In addition to serum iron levels, several tests may be ordered including UIBC, total iron binding capacity (TIBC) and ferritin. TIBC is a surrogate for transferrin and has a direct relationship to it. TIBC = (UIBC + serum iron).[1, 2, 3]

UIBC and TIBC are increased in low iron states such as uncomplicated anemia and decreased in high iron conditions such as hemochromatosis. The lone exception to the preceding is the case of anemia of chronic disease where the patient may be anemic but has adequate iron reserves and a low UIBC.[1]

Principles of the Procedure

Sample is added to an alkaline buffer containing a known concentration of iron to saturate the available binding sites on transferrin. The iron that remains free after transferrin saturation is reduced to a ferrous state and then complexed by Ferene-S* to form a stable complex, of which the color intensity is measured at 604 nm. The color intensity is directly proportional to the unbound excess iron concentration and indirectly proportional to the unsaturated iron-binding capacity. UIBC is therefore determined by subtracting the quantity of unbound iron from the total added quantity.

* Ferene-S = 3-(2-pyridyl)-5,6-bis-[2-(5-furylsulfonic acid)]-1,2,4- triazine

Methodology: Ferene

For additional information on system and assay technology, **refer to the Alinity ci-series Operations Manual, Section 3.**

REAGENTS

Kit Contents

Alinity c UIBC Reagent Kit 08P44

Volumes (mL) listed in the table below indicate the volume per cartridge.

REF	**08P4420**
Tests per cartridge	150
Number of cartridges per kit	2
Tests per kit	300
R1	32.9 mL
R2	12.3 mL
R1 Active ingredients: Glycyl glycine buffer (pH 8.6) (255 mmol/L), Sodium bicarbonate (46 mmol/L), Iron (II) chloride (20 µmol/L). Inactive ingredients: stabilizers, preservatives, and detergents.	
R2 Ascorbic acid (pH 2.5) (300 mmol/L), Ferene-S (12.5 mmol/L). Inactive ingredients: stabilizers, preservatives, and detergents.	

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

- Rx ONLY

Safety Precautions

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. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[4], [5], [6], [7]

The following warnings and precautions apply to: R1 and R2	
	
WARNING	Contains methylisothiazolone.
H317	May cause an allergic skin reaction.
Prevention	
P261	Avoid breathing mist / vapors / spray.
P272	Contaminated work clothing should not be allowed out of the workplace.
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.

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

Safety Data Sheets are available at www.corelaboratory.abbott or/and SDS folder.

For a detailed discussion of safety precautions during system operation, **refer to the Alinity ci-series Operations Manual, Section 8.**

Reagent Handling

- Reagents are shipped on wet ice.
- Upon receipt, place reagent cartridges in an upright position for 8 hours before use to

allow bubbles that may have formed to dissipate.

- If a reagent cartridge is dropped, place in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results.

For a detailed discussion of reagent handling precautions during system operation, refer to the Alinity ci-series Operations Manual, Section 7.

Reagent Storage

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position. May be used immediately after removal from 2 to 8°C storage.
Onboard	System Temperature	28 days	After 28 days (672 hours), the reagent kit must be discarded.
Opened	2 to 8°C	Until expiration date	Store in upright position. Do not reuse containers, original reagent caps, or replacement caps due to the risk of contamination and the potential to compromise reagent performance.

Reagents may be stored on or off the system. If removed from the system, store reagents with new replacement caps in an upright position at 2 to 8°C. For reagents stored off the system, it is recommended that they be stored in their original trays or boxes to ensure they remain upright.

For information on unloading reagents, **refer to the Alinity ci-series Operations Manual, Section 5.**

Indications of Reagent Deterioration

Deterioration of the reagents may be indicated when:

- a calibration error occurs
- a control value is out of the specified range

Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary.

For troubleshooting information, **refer to the Alinity ci-series Operations Manual, Section 10**.

INSTRUMENT PROCEDURE

The Alinity c UIBC assay file must be installed on the Alinity c analyzer prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the **Alinity ci-series Operations Manual, Section 2**.

For information on printing assay parameters, refer to the **Alinity ci-series Operations Manual, Section 5.**

For a detailed description of system procedures, **refer to the Alinity ci-series Operations Manual.**

Alternate Result Units

Edit assay parameter "Result Units" to select an alternate unit.

Conversion formula:

(Concentration in Default result unit) x (Conversion factor) =
(Concentration in Alternate result unit)

Default Result Unit	Conversion Factor	Alternate Result Unit
µg/dL	0.1798	µmol/L

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below were verified for use with this assay.

Other specimen types, collection tube types, and anticoagulants have not been verified with this assay.

Specimen Type	Collection Vessel
Serum	Serum tubes (with or without gel barrier)
Plasma	Collection tubes Acceptable anticoagulants are: Lithium heparin (with or without gel barrier) Sodium heparin

- Ethylenediaminetetraacetic acid (EDTA) and sodium fluoride/oxalate are not acceptable anticoagulants.9
- The instrument does not provide the capability to verify specimen types. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- For accurate results, plasma specimens should be free of platelets and other particulate matter. Ensure centrifugation is adequate to remove platelets.
- For additional information on specimen conditions, refer to the Interference section of this package insert.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

Serum: Ensure complete clot formation has taken place prior to centrifugation. Centrifuge according to tube manufacturer's specifications to ensure proper separation of serum from blood cells.

Plasma: Centrifuge according to tube manufacturer's specifications to remove platelets and ensure proper separation of plasma from blood cells.

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Specimens should be free of bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

To ensure consistency in results, recentrifuge specimens prior to testing if

- they contain fibrin, red blood cells, or other particulate matter.

NOTE: If fibrin, red blood cells, or other particulate matter are observed, mix by low speed vortex or by inverting 10 times prior to recentrifugation.

Prepare frozen specimens as follows:

- Frozen specimens must be completely thawed before mixing.
- Mix thawed specimens thoroughly.
- Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous.
- If specimens are not mixed thoroughly, inconsistent results may be obtained.
- NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

Specimen Storage

Specimen Type	Temperature	Maximum Storage Time
Serum/Plasma	20 to 25°C	7 days[10]
	2 to 8°C	3 weeks[10], [11]

Specimen Type	Temperature	Maximum Storage Time
	-20°C	1 year[10]

Avoid multiple freeze/thaw cycles.

Guder et al. suggest storage of frozen specimens at -20°C for no longer than the time intervals cited above.[10]

Each laboratory may establish a range around -20°C from either the freezer manufacturer's specifications or your laboratory standard operating procedure(s) for specimen storage.

Stored specimens must be inspected for particulates. If present, mix with a low speed vortex or by inversion and centrifuge the specimen to remove particulates prior to testing.

Specimen Shipping

Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

PROCEDURE

Materials Provided

08P44Alinity c UIBC Reagent Kit

Materials Required but not Provided

- Alinity c UIBC assay file
- 08P4401 Alinity c UIBC Calibrator Kit
- Commercially available controls
- Saline (0.85% to 0.90% NaCl) for specimen dilution

For information on materials required for operation of the instrument, **refer to the Alinity ci-series Operations Manual, Section 1.**

For information on materials required for maintenance procedures, **refer to the Alinity ci-series Operations Manual, Section 9.**

Assay Procedure

For a detailed description of how to run an assay, **refer to the Alinity ci-series Operations Manual, Section 5.**

- If using primary or aliquot tubes, refer to the Alinity ci-series Operations Manual, Section 4 to ensure sufficient specimen is present.
- To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.
- Minimum sample volume requirements:
  - Sample volume for single test: 25 µL.

    NOTE: This amount does not include the dead volume plus the additional over-

aspiration volume. **For total sample volume requirements, refer to the Alinity ci-series Operations Manual, Section 4.**

- Refer to the Alinity c UIBC Calibrator Kit package insert and commercially available control material package insert for preparation and usage.
- For general operating procedures, **refer to the Alinity ci-series Operations Manual, Section 5.**
- For optimal performance, it is important to perform routine maintenance as described in the **Alinity ci-series Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.**

Sample Dilution Procedures

Samples with UIBC values exceeding 500 µg/dL (89.5 µmol/L) are flagged with the code "> 500 µg/dL" (> 89.5 µmol/L) and may be diluted with the Manual Dilution Procedure.

Manual Dilution Procedure

Dilute the sample with saline (0.85% to 0.90% NaCl).

The operator must enter the dilution factor in the Specimen or Control tab of the Create Order screen. The system will use this dilution factor to automatically calculate the concentration of the sample and report the result.

If the operator does not enter the dilution factor, the result must be manually multiplied by the appropriate dilution factor before reporting the result. If a diluted sample result is less than the lower value of the measuring interval of 500 µg/dL (89.5 µmol/L), do not report the result. Rerun using an appropriate dilution.

For detailed information on ordering dilutions, refer to the Alinity ci-series Operations Manual, Section 5.

Calibration

For instructions on performing a calibration, refer to the Alinity ci-series Operations Manual, Section 5.

NOTE: The calibrator value for the Alinity c UIBC Calibrator must be entered as a negative number.

Calibration is stable for approximately **7 days (168 hours),** but is required with each **change in reagent cartridge**. Verify calibration with at least 2 levels of controls according to the laboratory quality control procedure. If control results fall outside acceptable ranges, recalibration may be necessary.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed.

Quality Control Procedures

- At least two levels of controls (normal and abnormal) are to be run every day testing performed.
- If quality control results do not meet the acceptance criteria defined by laboratory quality controls procedure, sample results may be suspect. Follow laboratory quality control

procedures to troubleshoot. Recalibration may be necessary. For troubleshooting information**, refer to the Alinity ci-series Operations Manual, Section 10.**

- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Commercial controls should be used according to the guidelines and recommendations of the control manufacturer. Concentration ranges provided in the control package insert should be used only for guidance.

For any control material in use, the laboratory should ensure that the matrix of the control material is suitable for use in the assay per the assay package insert.

Quality Control Guidance

Refer to "Basic QC Practices" by James O Westgard, Ph.D. for guidance on laboratory quality control practices.[12]

Verification of Assay Claims

For protocols to verify package insert claims, **refer to Verification of Assay Claims in the Alinity ci-series Operations Manual.**

RESULTS

Calculation

The Alinity c UIBC assay utilizes the Linear data reduction method to generate a calibration and results.

For information on alternate result units, refer to the INSTRUMENT PROCEDURE, Alternate Result Units section of this package insert.

Flags

Some results may contain information in the Flags field. For a description of the flags that may appear in this field, **refer to the Alinity ci-series Operations Manual, Section 5.**

Measuring Interval

Measuring interval is defined as the range of values in µg/dL (µmol/L) which meets the limits of acceptable performance for linearity, imprecision, and bias.

The measuring interval of the Alinity c UIBC assay is **25 µg/dL to 500** µg/dL (4.5 µmol/L to 89.5 µmol/L).

LIMITATIONS OF THE PROCEDURE

Use disposable plastic pipettes or glassware soaked in 1 N hydrochloric acid solution and rinsed with distilled water.

For diagnostic purposes, the test findings should always be assessed in conjunction with the patient's medical history, clinical examinations, and other findings.

Significant interference may be observed with hemolyzed samples. See Interference section for additional information.

Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS and SPECIFIC PERFORMANCE CHARACTERISTICS sections of this package insert.

EXPECTED VALUES

This study was performed on the ARCHITECT c System.

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

This laboratory will adopt manufacturer provided reference ranges. Effort will be made to verify it in house.

Reference Range

Serum and Plasma

	Range (µg/dL)	Range (µmol/L)
Male	69 to 240	12.4 to 43.0
Female	70 to 310	12.5 to 55.5

A confirmation study was conducted using 22 male and 22 female volunteers from a healthy donor population in Milan, Italy. Data were analyzed as described by Clinical and Laboratory Standards Institute (CLSI) protocol EP28-A3c.*13* From this study, the central 90% of specimens fell within the ranges above.

The circulated iron level can show a 30% diurnal variation, with a peak early in the morning.*14*

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

The Alinity c analyzer and the ARCHITECT c System utilize the same reagents and sample/reagent ratios.

Unless otherwise specified, all studies were performed on the Alinity c analyzer.

Precision

Within-Laboratory Precision

A study was performed based on guidance from CLSI EP05-A2.[15] Testing was conducted using 1 lot of the Alinity c UIBC Reagent Kit, 1 lot of the Alinity c UIBC Calibrator Kit, and 1 lot of commercially available controls, and 1 instrument. Three controls were assayed in a minimum of 2 replicates at 2 separate times per day on 20 different days.

Sample	n	Mean (µg/dL)	Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
			SD	%CV	SD	%CV
Control Level 1	120	150	2.4	1.6	4.9	3.3
Control Level 2	120	208	2.9	1.4	5.9	2.8
Control Level 3	120	267	2.8	1.0	5.0	1.9

Sample	n	Mean (µmol/L)	Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
			SD	%CV	SD	%CV
Control Level 1	120	26.8	0.43	1.6	0.88	3.3
Control Level 2	120	37.2	0.51	1.4	1.05	2.8
Control Level 3	120	47.9	0.50	1.1	0.89	1.9

[a] Includes within-run, between-run, and between-day variability.

Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.[16] Testing was conducted using 3 lots of the Alinity c UIBC Reagent Kit on each of 2 instruments over a minimum of 3 days. The Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) values are summarized below. These representative data support the lower limit of the measuring interval.

	µg/dL	µmol/L
LoB[a]	8	1.4
LoD[b]	13	2.3
LoQ[c,d]	**≤ 25**	≤ 4.5

[a] The LoB represents the 95th percentile from n ≥ 60 replicates of zero-analyte samples.

[b] The LoD represents the lowest concentration at which the analyte can be detected with 95% probability based on n ≥ 60 replicates of low-analyte level samples.

[c] The LoQ is defined as the lowest concentration at which a maximum allowable precision of 20 %CV was met.

[d] This value represents the claimed LoQ on the ARCHITECT System. The LoQ observed on the Alinity c analyzer supports this LoQ.

Linearity

A study was performed based on guidance from CLSI EP06-A.[17]

This assay is linear across the measuring interval of **25 µg/dL to 500** µg/dL (4.5 µmol/L to 89.5 µmol/L).

Interference

This study was performed on the ARCHITECT c System.

Potentially Interfering Substances and Potentially Interfering Drugs

A study was performed based on guidance from CLSI EP07-A2.[18] Representative data are summarized below.

Interference studies were conducted using an acceptance criteria of ± 10% or ± 14 µg/dL (2.5 µmol/L) deviation, whichever is greater, from the target. UIBC is not affected by the presence of the following interferents up to the concentrations indicated below.

Interfering Substance	Interferent Concentration	N	UIBC-Target (µg/dL)	Difference from Target (µg/dL)	%Difference from Target
Bilirubin (conjugated)	59 mg/dL	12	141	-10.6	—
	62 mg/dL	12	298	—	-4.0
Bilirubin (unconjugated)	53 mg/dL	12	156	—	-1.8
	56 mg/dL	12	284	—	-2.5
Copper	1000 µg/dL	3	139	-6.0	—
	2000 µg/dL	3	289	—	-7.8
Hemoglobin	62 mg/dL	12	168	—	-8.1
	125 mg/dL	12	323	—	-9.4
Intralipid	1000 mg/dL	12	142	-9.7	—
	1000 mg/dL	12	295	—	-1.6
Oxytetracycline	40 mg/L	3	145	—	7.9
	100 mg/L	3	291	—	4.9
Rheumatoid Factor	100 IU/mL	3	145	—	2.4

Interfering Substance	Interferent Concentration	N	UIBC-Target (µg/dL)	Difference from Target (µg/dL)	%Difference from Target
	100 IU/mL	3	300	—	-0.2
Triglycerides*	901 mg/dL	12	147	—	-2.8
	1157 mg/dL	12	269	—	-6.7
Total Protein	13.2 g/dL	12	152	—	5.2
	13.4 g/dL	12	252	—	10.0

Interfering Substance	Interferent Concentration	N	UIBC-Target (µmol/L)	Difference from Target (µmol/L)	%Difference from Target
Bilirubin (conjugated)	1008.9 µmol/L	12	25.2	-1.9	—
	1060.2 µmol/L	12	53.3	—	-4.0
Bilirubin (unconjugated)	906.3 µmol/L	12	27.9	—	-1.8
	957.6 µmol/L	12	50.8	—	-2.5
Copper	157.0 µmol/L	3	24.9	-1.1	—
	314.0 µmol/L	3	51.7	—	-7.8
Hemoglobin	0.62 g/L	12	30.1	—	-8.1
	1.25 g/L	12	57.8	—	-9.4
Intralipid	10 g/L	12	25.4	-1.7	—
	10 g/L	12	52.8	—	-1.6
Oxytetracycline	81 µmol/L	3	26.0	—	7.9
	220 µmol/L	3	52.1	—	4.9
Rheumatoid Factor	100 IU/mL	3	26.0	—	2.4
	100 IU/mL	3	53.7	—	-0.2
Triglycerides*	10.2 mmol/L	12	26.3	—	-2.8
	13.1 mmol/L	12	48.2	—	-6.7
Total Protein	132 g/L	12	27.2	—	5.2
	134 g/L	12	45.1	—	10.0

* Triglycerides testing was performed using commercially available, human-sourced lipemic material. The results displayed here may not adequately represent results observed on other instruments with similarly-sourced, but different lipemic material.[19, 20]

Clinical samples with high triglycerides can be clear while samples with moderate triglycerides can be turbid. The light scatter for Intralipid does not always match with that of lipoproteins in the patient samples due to differences in the size and distribution of these lipoproteins.[21]

The effect of interfering substances has only been evaluated for those listed above.

The following compounds may interfere with the UIBC assay:

- **Gadolinium Magnetic Resonance Contrast Agents[22, 23]**
- **Deferasirox[24]**

Interferences from medication or endogenous substances may affect results.

Method Comparison

A study was performed based on guidance from CLSI EP09-A3[25] using the Passing-Bablok regression method.

		Units	n	Correlation Coefficient	Intercept	Slope	Concentration Range
Alinity c UIBC vs ARCHITECT UIBC	Serum	µg/dL	111	1.00	-6.56	1.00	42 - 500
		µmol/L	111	1.00	-1.21	1.00	7.5 - 89.4

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