Alinity c Carbon Dioxide-09

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SUPERSEDES: Procedure titled _____

INTENDED USE

The Alinity c Carbon Dioxide assay is used for the quantitation of carbon dioxide in human serum or plasma on the Alinity c analyzer.

SUMMARY AND EXPLANATION OF THE TEST

The determination of serum carbon dioxide total (CO_2) in conjunction with other clinical and laboratory information is necessary for the evaluation of acid-base status. A high CO_2 content may be observed in compensated respiratory acidosis and metabolic alkalosis. A low CO_2 content may be observed in compensated respiratory alkalosis and metabolic acidosis. Additional laboratory determinations will permit differentiation between metabolic and respiratory conditions.[1]

PRINCIPLES OF THE PROCEDURE

Carbon dioxide, as bicarbonate (HCO_3^-), and phospho(enol)pyruvate (PEP) are converted to oxalacetate and phosphate in the reaction catalyzed by phospho(enol)pyruvate carboxylase (PEPC). Malate dehydrogenase (MDH) catalyzes the reduction of oxalacetate to malate with the concomitant oxidation of reduced nicotinamide adenine dinucleotide (NADH) analog.[2] The resulting decrease in absorbance at 404 nm is proportional to the CO_2 content in the sample.

Methodology: PEP Carboxylase

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

REAGENTS

Kit Contents

Alinity c Carbon Dioxide Reagent Kit 07P72

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

REF	**07P7220**
Tests per cartridge	300
Number of cartridges per kit	10
Tests per kit	3000
R1	20.7 mL
R1 Active ingredients: Phospho(enol)pyruvate (63 mmol/L), NADH analog (3.0 mmol/L), Phospho(enol)pyruvate carboxylase (microbial) (> 2000 U/L), and Malate dehydrogenase (mammalian) (> 20 000 U/L). Preservative: sodium azide (0.08%).	

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.[3], [4], [5], [6]

The following warnings and precautions apply to: R1	
Contains Tris hydroxymethyl aminomethane* and sodium azide.	
H316*	Causes mild skin irritation.
EUH032	Contact with acids liberates very toxic gas.
Response	
P332+P313*	If skin irritation occurs: 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.

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 the Alinity ci-series Operations Manual, Section 8.

Reagent Handling

- Reagents are shipped refrigerated or on cold packs.
- Upon receipt, place reagent cartridges in an upright position for 1 hour 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.
Onboard	System Temperature	14 days	
Opened	2 to 8°C	Until expiration date	Store in upright position. Do not reuse 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 Carbon Dioxide 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
mEq/L	1	mmol/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

- 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

- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- For accurate results, plasma specimens should be free of platelets and other particulate matter. Ensure centrifugation is adequate to remove platelets.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- 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.

Specimen Storage

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
Serum/Plasma	20 to 25°C	SST, LiH, NaH: 2 hours[9]	Keep tube tightly capped for storage.[7]
		SER, PST: 8 hours[9]	A consequent decrease in the CO_2 value of up to **6 mEq/L** can occur in the course of an hour once the specimen has
	2 to 8°C	LiH: 2 days[9]	
		SER, SST, PST,	

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
		NaH: 3 days[9]	been exposed to ambient air.[8]
	-20°C	2 weeks[10]	

SER: Serum Tube

SST: Serum Separator Tube

PST: Plasma Separator Tube (Lithium Heparin)

LiH: Lithium Heparin (without gel)

NaH: Sodium Heparin

If analysis will not be completed within the maximum storage recommendations, the separated serum/plasma should be frozen at or below -20°C. For additional information on sample handling and processing, refer to CLSI GP44-A4.[11] Repeated freeze/thaw cycles should be avoided to minimize analyte deterioration. The storage information provided here is based on references or data maintained by the manufacturer.

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

07P72 Alinity c Carbon Dioxide Reagent Kit

Materials Required but not Provided

- Alinity c Carbon Dioxide assay file
- 08P7201 Alinity c Carbon Dioxide Calibrator Kit
- Commercially available controls containing carbon dioxide
- 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: 1.5 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 Carbon Dioxide 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 a carbon dioxide value exceeding 50 mEq/L (50 mmol/L) are flagged with the code "> 50 mEq/L" (> 50 mmol/L) and may be diluted with either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a **1:2** dilution of the sample and automatically calculates the concentration by multiplying the result by the dilution factor.

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 5 mEq/L (5 mmol/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.

Calibration is stable for approximately **14 days (336 hours),** but is required with each change

in reagent lot. Verify calibration with at least 2 levels of controls according to the established quality control requirements for your laboratory. 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

- 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 the established 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 Carbon Dioxide 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 mEq/L (mmol/L) which meets the limits of acceptable performance for linearity, imprecision, and bias.

The measuring interval of the Alinity c Carbon Dioxide assay is 5 to 50 mEq/L (**5 to 50 mmol/L**).

LIMITATIONS OF THE PROCEDURE

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

Abnormally elevated or fluctuating CO_2 levels in the laboratory may interfere with carbon dioxide measurements, leading to inaccurate results. Under these circumstances, more frequent calibrations may be necessary.

EXPECTED VALUES

It is recommended that each laboratory determine its own reference range based upon its particular locale and population characteristics.

Reference Range

Serum/Plasma*13*

	Range (mEq/L)
Cord	14 to 22
Newborn	13 to 22
Premature, 1 week	14 to 27
Infant	20 to 28
Child	20 to 28

	Range (mEq/L)
Adult	22 to 29
> 60 years	23 to 31

For Carbon Dioxide, results expressed in mEq/L are equivalent to mmol/L.

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 and AEROSET 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.*14* Testing was conducted using 1 lot of the Alinity c Carbon Dioxide Reagent Kit, 1 lot of the Alinity c Carbon Dioxide Calibrator Kit, 1 lot of commercially available controls, and 1 instrument. Three control levels were assayed in a minimum of 2 replicates at 2 separate times per day on 20 different days.

			Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
Sample	**N**	**Mean mEq/L (mmol/L)**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	120	18	0.4	2.0	0.6	3.6
Control Level 2	120	22	0.5	2.1	0.9	3.9
Control Level 3	119	33	0.7	2.2	1.1	3.3

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

Accuracy

This study was performed on the ARCHITECT c System.

Representative data from studies using NIST traceable standards and comparing results with the NIST certified concentration are summarized below.

N	20
Concentration (mEq/L)	20

Mean Bias (mEq/L)	-0.7
Mean Bias (%)	-3.7
Total Error (%)	8.0

Lower Limits of Measurement

A study was performed based on guidance from CLSI EP17-A2.*15* Testing was conducted using 3 lots of Alinity c Carbon Dioxide Reagent Kits 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.

	mEq/L (mmol/L)
LoB[a]	2
LoD[b]	3
LoQ[c, d]	**4**

[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 observed 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.*16*

This assay is linear across the measuring interval of 5 to 50 mEq/L (**5 to 50 mmol/L**).

Interference

Interference studies were conducted using an acceptance criteria of ± 4.3% or 1 mEq/L, whichever is greater, from the target value.

This study was performed on the AEROSET System.

Potentially Interfering Endogenous Substances

Interference effects were assessed by Dose Response method, at the medical decision levels of the analyte.

Potentially Interfering Substance	**Lower Decision Level**			
	Interferent Level		**Target Level**	**Recovery (% of Target)***
	Default Units	**Alternate Units**		
Bilirubin	30 mg/dL	513 µmol/L	20.5 mEq/L	100
	60 mg/dL	1026 µmol/L	20.5 mEq/L	99
Hemoglobin	1000 mg/dL	10 g/L	20.1 mEq/L	99

Potentially Interfering Substance	Lower Decision Level			
	Interferent Level		Target Level	Recovery (% of Target)*
	Default Units	Alternate Units		
	2000 mg/dL	20 g/L	20.1 mEq/L	95
Intralipid	1000 mg/dL	10 g/L	20.0 mEq/L	100
	2000 mg/dL	20 g/L	20.0 mEq/L	102

Potentially Interfering Substance	Upper Decision Level			
	Interferent Level		Target Level	Recovery (% of Target)*
	Default Units	Alternate Units		
Bilirubin	30 mg/dL	513 µmol/L	36.9 mEq/L	101
	60 mg/dL	1026 µmol/L	36.9 mEq/L	100
Hemoglobin	1000 mg/dL	10 g/L	34.9 mEq/L	102
	2000 mg/dL	20 g/L	34.9 mEq/L	101
Intralipid	1000 mg/dL	10 g/L	36.8 mEq/L	99
	2000 mg/dL	20 g/L	36.8 mEq/L	98

*Percentages have been rounded to whole numbers.

The following drugs were tested on the ARCHITECT c System for interference at the concentrations indicated using an acceptance criteria of ± 4.3% or 1 mEq/L, whichever is greater, from the target value.

Potentially Interfering Substance	Interferent Level		Target Level	Recovery (% of Target)
	Default Units	Alternate Units		
Sulfapyridine	300 mg/L	1204.8 µmol/L	20.4 mEq/L	100
Sulfasalazine	300 mg/L	753.8 µmol/L	20.4 mEq/L	98.5
Temozolomide	20 mg/L	103.1 µmol/L	18.9 mEq/L	102

Interferences from medication or endogenous substances may affect results.[17]

Method Comparison

A study was performed based on guidance from CLSI EP09-A3 using the Passing-Bablok regression method.[18]

		Units	n	Correlation Coefficient	Intercept	Slope	Concentration Range
Alinity c Carbon Dioxide vs ARCHITECT Carbon Dioxide	Plasma	mEq/L (mmol/L)	114	1.00	1.00	1.00	5 - 46

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