Alinity c Creatine Kinase (CK)-10

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SUPERSEDES: Procedure titled _____

INTENDED USE

The Alinity c Creatine Kinase assay is used for the quantitation of creatine kinase in human serum or plasma on the Alinity c analyzer.

SUMMARY AND EXPLANATION OF THE TEST

Measurements of creatine kinase are used in the diagnosis and treatment of diseases associated with skeletal muscle, heart, central nervous system, and thyroid.

PRINCIPLES OF THE PROCEDURE

Creatine kinase (CK), present in the sample, catalyzes the transfer of a high energy phosphate group from creatine phosphate to ADP. The ATP produced in this reaction is subsequently used to phosphorylate glucose to produce glucose-6-phosphate (G-6-P) in the presence of hexokinase. G-6-P is then oxidized by glucose-6-phosphate dehydrogenase (G-6-PDH) with the concomitant reduction of nicotinamide adenine dinucleotide phosphate (NADP) to nicotinamide adenine dinucleotide phosphate reduced (NADPH). The rate of formation of NADPH is monitored at 340 nm and is proportional to the activity of CK in the sample. These reactions occur in the presence of N-acetyl-L-cysteine (NAC) which is present as an enzyme reactivator.

Methodology: NAC (N-acetyl-L-cysteine)

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

REAGENTS

Kit Contents

Alinity c Creatine Kinase Reagent Kit 08P42

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

REF	**08P4220**
Tests per cartridge	300
Number of cartridges per kit	4
Tests per kit	1200
R1	35.8 mL
R2	12.0 mL
R1 Active ingredients: ADP potassium salt (2.55 mmol/L), AMP (6.37 mmol/L), AP5A (0.0127 mmol/L), β-NADP (2.54 mmol/L), EDTA (2.0 mmol/L), G-6-PDH (Leuconostoc mesenteroides) (1.95 U/mL), Glucose (0.2 mmol/L), Hexokinase (yeast) (3.9 U/mL), Imidazole (100 mmol/L), Magnesium acetate (10 mmol/L), and NAC (25.5 mmol/L). Preservative: sodium azide (0.1 %).	
R2 Active ingredients: Creatine phosphate (153 mmol/L), Glucose (99.2 mmol/L), Imidazole (100 mmol/L), and Magnesium acetate (10 mmol/L). Preservative: sodium azide (0.1 %).	

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.[1], [2], [3], [4]

The following warnings and precautions apply to: R1	
	
DANGER	Contains imidazole and sodium azide.

H360	May damage fertility or the unborn child.
H316*	Causes mild skin irritation.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P201	Obtain special instructions before use.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P308+P313	IF exposed or concerned: Get medical advice / attention.
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.

The following warnings and precautions apply to: R2	
	
DANGER	Contains imidazole and sodium azide.
H360	May damage fertility or the unborn child.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P201	Obtain special instructions before use.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P308+P313	IF exposed or concerned: Get medical advice / attention.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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/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

·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	30 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 Creatine Kinase 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.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

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

Other specimen types and collection tube types/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

·To ensure accurate results, the plasma specimen tube should be filled with the prescribed minimum volume for an appropriate anticoagulant to specimen ratio.[5]

·NOTE: **Moderate** or **severely hemolyzed** specimens can liberate adenylate kinase, ATP, and G-6-P which may affect the **lag phase and side reactions of the CK** assay system.[6]

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
Serum/Plasma	20 to 25°C	2 days[7]
	2 to 8°C	7 days[7, 8]

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.

Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

08P42 Alinity c Creatine Kinase Reagent Kit

Materials Required but not Provided

·Alinity c Creatine Kinase assay file

·Commercially available controls containing creatine kinase

·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: 2.5 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 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 creatine kinase value exceeding 4267 U/L are flagged with the code ">4267 U/L" and may be diluted with either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a **1:10** 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 7 U/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 **30 days (720 hours),** but is required with each change in reagent lot. Verify calibration with at least 2 levels of controls according to the laboratory established 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

- 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.[9]

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 Creatine Kinase assay utilizes the **Factor data reduction** method to generate a calibration and results. The calibration factor for the Alinity c Creatine Kinase assay is **9081**.

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 U/L which meets the limits of acceptable performance for linearity, imprecision, and bias.

The measuring interval of the Alinity c Creatine Kinase assay is **7 U/L to 4267** U/L.

LIMITATIONS OF THE PROCEDURE

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

EXPECTED VALUES

Manufacturer reference range will be used. Effort will be made to verify locally.

Reference Range

Serum/Plasma[10]

	Range (U/L)
Male	30 to 200
Female	29 to 168

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. Testing was conducted using 1 lot of the Alinity c Creatine Kinase Reagent Kit, 1 lot of commercially available controls, and 1 instrument. Three controls and one panel were assayed in a minimum of 2 replicates at 2 separate times per day on 20 different days.[11]

			Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
Sample	**n**	**Mean (U/L)**	**SD**	**%CV**	**SD**	**%CV**
Control Level 1	120	63	1.0	1.5	1.0	1.6
Control Level 2	120	241	1.6	0.6	2.3	0.9
Control Level 3	120	431	4.2	1.0	5.4	1.2
Panel	119	148	1.5	1.0	1.6	1.1

[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. Testing was conducted using 3 lots of the Alinity c Creatine Kinase Reagent Kit on each of 2 instruments over a minimum of 3 days. The maximum observed Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) values are summarized below.[12]

	U/L
LoB[a]	3
LoD[b]	5
LoQ[c]	**7**

[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 was determined from n ≥ 60 replicates of low-analyte level samples and is defined as the lowest concentration at which a maximum allowable precision of 20 %CV was met.

Linearity

A study was performed based on guidance from CLSI EP06-A.[13]

This assay is linear across the measuring interval of **7 to 4267 U/L**.

Interference

This study was performed on the AEROSET System.

Potentially Interfering Endogenous Substances

Interference studies were conducted using NCCLS EP7-P.[14] Interference effects were assessed by Dose Response and Paired Difference methods, at the medical decision level of the analyte.

Potentially Interfering Substance	**Interferent Level**		**Creatine Kinase Target Level**	
	Default Units	**Alternate Units**	**U/L**	**Recovery (% of Target)**
Bilirubin	30 mg/dL	513 µmol/L	201.2	94.3
	60 mg/dL	1026 µmol/L	201.2	100.5
Hemoglobin	1000 mg/dL	10 g/L	178.8	100.6
	2000 mg/dL	20 g/L	178.8	102.4
Intralipid	750 mg/dL	7.5 g/L	189.0	99.3

Potentially Interfering Substance	Interferent Level		Creatine Kinase Target Level	
	Default Units	Alternate Units	U/L	Recovery (% of Target)
	1000 mg/dL	10 g/L	189.0	97.9

The following drugs were tested on the ARCHITECT system for interference at the concentrations indicated using an acceptance criteria of ± 10% from the target value.

Potentially Interfering Substance	Interferent Level		Creatine Kinase Target Level	
	Default Units	Alternate Units	U/L	Recovery (% of Target)
Sulfapyridine	300 mg/L	1204.8 µmol/L	114.7	100.4
Sulfasalazine	300 mg/L	753.8 µmol/L	114.7	103.7
Temozolomide	20 mg/L	103.1 µmol/L	209.4	100.0

Interferences from medications or endogenous substances may affect results.[15]

Method Comparison

A study was performed based on guidance from CLSI EP09-A3 using the Passing-Bablok regression method.[16]

		Units	n	Correlation Coefficient	Intercept	Slope	Concentration Range
Alinity c Creatine Kinase vs ARCHITECT Creatine Kinase	Serum	U/L	124	1.00	-1.01	1.02	14-3844

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