ARCHITECT

CREATINE KINASE

This package insert contains information to run the Creatine Kinase assay on the ARCHITECT *c* Systems.

Revised February 2022.

Package insert instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Customer Service: Contact your local representative or find country-specific contact information on www.corelaboratory.abbott

Key to Symbols

ISO 15223 Symbols		Other Symbols	
	Consult instructions for use	CONTAINS: AZIDE	Contains sodium azide. Contact with acids liberates very toxic gas.
	Manufacturer	DISTRIBUTED IN THE USA BY	Distributed in the USA by
Σ	Sufficient for	FOR USE WITH	Identifies products to be used together
	Temperature limitation	INFORMATION FOR USA ONLY	Information needed for United States of America only
	Use by/Expiration date	MANUFACTURED FOR	Manufactured for
IVD	*In Vitro* Diagnostic Medical Device	PRODUCT OF JAPAN	Product of Japan
LOT	Batch code/Lot number	R1	Reagent 1
REF	Catalog number/List number	R2	Reagent 2
SN	Serial Number	Rx ONLY	For use by or on the order of a physician only (applicable to USA classification only)

Abbott

NAME

CREATINE KINASE

INTENDED USE

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

SUMMARY AND EXPLANATION OF 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 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)

REAGENTS

Reagent Kit

Creatine Kinase is supplied as a liquid, ready-to-use, two-reagent kit which contains:

REF **7D63-22**

- R1 5 x 48 mL
- R2 5 x 15 mL

Estimated tests per kit: 1250*

REF **7D63-42**

- R1 5 x 87 mL
- R2 5 x 27 mL

Estimated tests per kit: 2310*

*Calculation is based on the minimum reagent fill volume per kit.

Reactive Ingredients		Concentration
R1	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
	NAC	25.5 mmol/L
R2	Creatine phosphate	153 mmol/L
	Glucose	99.2 mmol/L
	Imidazole	100 mmol/L
	Magnesium acetate	10 mmol/L

Inactive Ingredients: R1 and R2 contain sodium azide (0.1%) as a preservative.

REAGENT HANDLING AND STORAGE

Reagent Handling

Remove air bubbles, if present in the reagent cartridge, with a new applicator stick. Alternatively, allow the reagent to sit at the appropriate storage temperature to allow the bubbles to dissipate. To minimize volume depletion, do not use a transfer pipette to remove the bubbles.

CAUTION: Reagent bubbles may interfere with proper detection of reagent level in the cartridge, causing insufficient reagent aspiration which could impact results.

Reagent Storage

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

Reagent stability is 30 days if the reagent is uncapped and onboard.

Indications of Deterioration

Instability or deterioration should be suspected if there are precipitates, visible signs of leakage, extreme turbidity, microbial growth, if calibration does not meet the appropriate package insert and/or **ARCHITECT System Operations Manual** criteria, or if controls do not meet the appropriate criteria.

WARNINGS AND PRECAUTIONS

Precautions for Users

- IVD
- For *In Vitro* Diagnostic Use.
- Rx ONLY
- Do not use components beyond the expiration date.
- Do not mix materials from different kit lot numbers.
- **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.[1] Biosafety Level 2[2] or other appropriate biosafety practices[3,4] should be used for materials that contain or are suspected of containing infectious agents.
- The following warnings and precautions apply to R1:

DANGER: Contains acetic acid*, 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 contact your local representative.
- For a detailed discussion of safety precautions during system operation, refer to the **ARCHITECT System Operations Manual,** *Section 8*.

SPECIMEN COLLECTION AND HANDLING

Suitable Specimens

Serum and plasma are acceptable specimens.

- **Serum:** Use serum collected by standard venipuncture techniques into glass or plastic tubes with or without gel barriers. Ensure complete clot formation has taken place prior to centrifugation. Centrifuge according to tube manufacturer's instructions to ensure proper separation of serum from blood cells.

  Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may take longer to complete their clotting processes. Fibrin clots may subsequently form in these sera and the clots could cause erroneous test results.
- **Plasma:** Use plasma collected by standard venipuncture techniques into glass or plastic tubes. Acceptable anticoagulants are lithium heparin (with or without gel barrier) and sodium heparin. Ensure centrifugation is adequate to remove platelets. Centrifuge according to tube manufacturer's instructions to ensure proper separation of plasma from blood cells. 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]

For total sample volume requirements, refer to the ASSAY PARAMETERS section of this package insert and *Section 5* of the **ARCHITECT System Operations Manual**.

Specimen Storage

Serum and Plasma

Temperature	Maximum Storage	Bibliographic Reference
20 to 25°C	2 days	7
2 to 8°C	7 days	7, 8

NOTE: Stored specimens must be inspected for particulates. If present, mix and centrifuge the specimen to remove particulates prior to testing.

PROCEDURE

Materials Provided

7D63 Creatine Kinase Reagent Kit

Materials Required but not Provided

- Control Material
- Saline (0.85% to 0.90% NaCl) for specimens that require dilution

Assay Procedure

For a detailed description of how to run an assay, refer to *Section 5* of the **ARCHITECT System Operations Manual**.

Specimen Dilution Procedures

The ARCHITECT *c* Systems have an automatic dilution feature; refer to *Section 2* of the **ARCHITECT System Operations Manual** for additional information.

Serum and Plasma: Specimens with creatine kinase values exceeding 4,267 U/L are flagged and may be diluted by following either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

If using the Automated Dilution Protocol, the system performs a 1:2 or 1:10 dilution of the specimen and automatically corrects the enzyme activity value by multiplying the result by the appropriate dilution factor.

Manual Dilution Procedure

Manual dilutions should be performed as follows:

- Use saline (0.85% to 0.90% NaCl) to dilute the sample.
- The operator must enter the dilution factor in the patient or control order screen. The system uses this dilution factor to automatically correct the enzyme activity value by multiplying the result by the entered factor.
- If the operator does not enter the dilution factor, the result must be multiplied by the appropriate dilution factor before reporting the result.

NOTE: If a diluted sample result is flagged indicating it is less than the linear low limit, do not report the result. Rerun using an appropriate dilution.

For detailed information on ordering dilutions, refer to *Section 5* of the **ARCHITECT System Operations Manual**.

CALIBRATION

Calibration is stable for approximately 30 days (720 hours) and is required with each change in reagent lot number. Verify calibration with at least two levels of controls according to the established quality control requirements for your laboratory. If control results fall outside acceptable ranges, recalibration may be necessary.

A calibration factor (9081) must be entered on the **Configure assay parameters** window, **Calibration** view.

For a detailed description of how to calibrate an assay, refer to *Section 6* of the **ARCHITECT System Operations Manual**.

QUALITY CONTROL

The following is the recommendation of Abbott Laboratories for quality control. As appropriate, refer to your laboratory standard operating procedure(s) and/or quality assurance plan for additional quality control requirements and potential corrective actions.

- Two levels of controls (normal and abnormal) are to be run every 24 hours.
- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, patient values may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary.
- Review quality control results and acceptance criteria following a change of reagent lot.

RESULTS

Refer to *Appendix C* of the **ARCHITECT System Operations Manual** for information on results calculations.

Representative performance data are given in the EXPECTED VALUES and SPECIFIC PERFORMANCE CHARACTERISTICS sections of this package insert. Results obtained in individual laboratories may vary.

LIMITATIONS OF THE PROCEDURE

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

EXPECTED VALUES

Reference Range

Serum/Plasma[9]

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

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

SPECIFIC PERFORMANCE CHARACTERISTICS

Linearity

Creatine Kinase is linear up to 4,267 U/L. Linearity was verified using Clinical and Laboratory Standards Institute (CLSI) protocol NCCLS EP6-P.[10]

Limit of Detection (LOD)

The LOD for Creatine Kinase is 5 U/L. The LOD is the mean concentration of an analyte-free sample + 2 SD, where SD = the pooled, within run standard deviation of the analyte-free sample.
A study performed on an ARCHITECT *c* System produced an LOD for Creatine Kinase of 5.1 U/L.

Limit of Quantitation (LOQ)

The LOQ for Creatine Kinase is 6.6 U/L. The LOQ is the analyte concentration at which the CV = 20%.

Interfering Substances

Interference studies were conducted using CLSI protocol NCCLS EP7-P.[11] Interference effects were assessed by Dose Response and Paired Difference methods, at the medical decision level of the analyte.

Interfering Substance	Interferent Concentration	N	Target (U/L)	Observed (% of Target)
Bilirubin	30 mg/dL (513 µmol/L)	4	201.2	94.3
	60 mg/dL (1,026 µmol/L)	4	201.2	100.5

Hemoglobin	1,000 mg/dL (10 g/L)	4	178.8	100.6
	2,000 mg/dL (20 g/L)	4	178.8	102.4
Intralipid	750 mg/dL (7.5 g/L)	4	189.0	99.3
	1,000 mg/dL (10.0 g/L)	4	189.0	97.9

Bilirubin solutions at the above concentrations were prepared by addition of a bilirubin stock to human serum pools. Hemoglobin solutions at the above concentrations were prepared by addition of hemolysate to human serum pools. Intralipid solutions at the above concentrations were prepared by addition of Intralipid to human serum pools.

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

Interfering Substance	Interferent Concentration	N	Target (U/L)	Observed (% of Target)
Sulfapyridine	300 mg/L (1204.8 µmol/L)	3	114.7	100.4
Sulfasalazine	300 mg/L (753.8 µmol/L)	3	114.7	103.7
Temozolomide	20 mg/L (103.1 µmol/L)	3	209.4	100.0

Interferences from medications or endogenous substances may affect results.[12]

Precision

The imprecision of the Creatine Kinase assay is ≤ 6.5% Total CV. Representative data from studies using CLSI protocol NCCLS EP5-A[13] are summarized below.

Control		Level 1	Level 2
N		80	80
Mean (U/L)		136.8	387.6
Within Run	SD	1.73	1.79
	%CV	1.3	0.5
Between Run	SD	2.00	3.48
	%CV	1.5	0.9
Between Day	SD	4.66	12.20
	%CV	3.4	3.2
Total	SD	5.36	12.81
	%CV	3.9	3.3

Method Comparison

Correlation studies were performed using CLSI protocol NCCLS EP9-A.[14]

Serum results from the Creatine Kinase assay on the AEROSET System were compared with those from a commercially available CK *N*-acetyl-*L*-cysteine methodology.

Serum results from the Creatine Kinase assay on an ARCHITECT *c* System were compared with those from the Creatine Kinase assay on the AEROSET System.

	AEROSET vs. Comparative Method	ARCHITECT vs. AEROSET
N	79	80
Y - Intercept	-0.829	-2.641
Correlation Coefficient	0.999	1.000
Slope	0.988	1.005
Range (U/L)*	7.9 to 2,200.0 U/L	9.9 to 3,778.3 U/L

*AEROSET Range

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Note for number formatting:

- A space is used as thousands separator (example: 10 000 specimens).
- A period is used to separate the integer part from the fractional part of a number written in decimal form (example: 3.12%).

TRADEMARKS

The ARCHITECT *c* System family of instruments consists of *c* 4000, *c* 8000, and *c* 16000 instruments.

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DISTRIBUTED IN THE USA BY
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Revised February 2022.

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ARCHITECT

Creatine Kinase Serum/Plasma—Conventional and SI Units

Configure assay parameters — General

● General O Calibration O SmartWash O Results O Interpretation

Assay: **CK** Type: **Photometric** Version: †
Number: **1026**
Run controls for onboard reagents by: **Lot**

● Reaction definition O Reagent / Sample O Validity checks

Reaction mode: **Rate up**

	Primary	Secondary		Read times
Wavelength:	**340**	/ ‡	Main:	**24 – 33**
Last required read:	**33**		Flex:	___ – ___
Absorbance range:	**0.0000 – 2.8000**		Color correction:	___ – ___
Sample blank type:	**Self**		Blank:	**10 – 16**

O Reaction definition ● Reagent / Sample O Validity checks

		R1	R2
Reagent:	**CK000**	Reagent volume:	**160**	**40**
Diluent:	**Saline**	Water volume:	___	___
Diluent dispense mode:	**Type 0**	Dispense mode:	**Type 0**	**Type 0**

Dilution name	Sample	Diluted sample	Diluent	Water		Dilution factor	Default dilution
STANDARD :	**4.0**	___	___	___	=	**1:1.00**	●
1:2 :	**2.0**	___	___	___	=	**1:1.98**	O
1:10 :	**10.0**	**4.0**	**90**	___	=	**1:10.00**	O

O Reaction definition O Reagent / Sample ● Validity checks

Reaction check: **Rate Subtraction**

	A	B
Read time:	**5 – 10**	**10 – 16**
Calculation limits:	**-0.0050 – 0.0050**	

Rate linearity %: **10**

Configure assay parameters — Calibration

O General ● Calibration O SmartWash O Results O Interpretation

Assay: **CK** Calibration method: **Factor**
Factor: **9081.0000**

● Calibrators O Volumes O Intervals O Validity checks

Calibrator set: **None** Calibrator level: Blank: **Water** Concentration: **0**

Replicates: **3** [Range 1 – 3]

O Calibrators ● Volumes O Intervals O Validity checks

Calibrator:

	Calibrator level	Sample	Diluted sample	Diluent	Water
Blank:	**Water**	**4.0**	___	___	___

O Calibrators O Volumes ● Intervals O Validity checks

Calibration intervals:
Full interval: **720** (hours)

O Calibrators O Volumes O Intervals ● Validity checks

Blank absorbance range: _____ – _____

Configure assay parameters — SmartWash

O General O Calibration ● SmartWash O Results O Interpretation

Assay: **CK**

COMPONENT	REAGENT / ASSAY	WASH	Volume	Replicates
Sample probe‡‡	___	**Detergent A**		

‡‡ Sample probe *Sample wash protocol* is **Maximum wash**.

Configure assay parameters — Results

O General O Calibration O SmartWash ● Results O Interpretation

Assay: **CK** Assay number: **1026**
Dilution default range: Result units: **U/L**
Low-Linearity: **7**††
High-Linearity: **4267**
Gender and age specific ranges:

GENDER	AGE (UNITS)	NORMAL	EXTREME
Male	**20 – 80 (Y)**	**30 – 200**	
Female	**20 – 80 (Y)**	**29 – 168**	

Configure result units

Assay: **CK**
Version: †
Result units: **U/L**
Decimal places: **0** [Range 0 – 4]
Correlation factor: **1.0000**
Intercept: **0.0000**

† Due to differences in instrument systems and unit configurations, version numbers may vary.
‡ *c*8000 Secondary Wavelength is 412 nm, *c*4000 and *c*16000 Secondary Wavelength is 416 nm.
†† The linear low value (Low-Linearity) is LOQ rounded up to the number of decimal places defined in the decimal places parameter field.