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ADVIA® Chemistry XPT
Systems

Creatine Kinase (CK_L)

Current Revision and Date[a]	Rev. A, 2016-10	
Product Name	ADVIA® Chemistry Creatine Kinase (CK_L) Reagents	REF 10729780 (1100 tests per kit)
Systems	ADVIA Chemistry XPT System	
Materials Required but Not Provided	Reagent container adapters Commercially available controls	
Specimen Types	Human serum, plasma (lithium heparin)	
Assay Principle	IFCC reference method	
Assay Range	Serum: 15–1300 U/L Plasma: 15–1300 U/L	
Reagent Storage	2–8°C	
Reagent On-System Stability	30 days	
Reagent Code	74034	

[a] In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

The ADVIA® Chemistry Creatine Kinase (CK_L) assay is for *in vitro* diagnostic use in the quantitative determination of creatine kinase activity in human plasma (lithium heparin) or serum on ADVIA Chemistry XPT systems. The assay can be used to aid in the diagnosis and treatment of myocardial infarction and muscle diseases, such as Duchenne progressive muscular dystrophy.

Summary and Explanation

The ADVIA Chemistry CK_L assay is an adaptation of the IFCC Reference Method. The reaction is based on the modified procedure of Szasz.[1,2]

Principles of the Procedure

Creatine Kinase reacts with creatine phosphate and adenosine diphosphate (ADP) to form adenosine triphosphate (ATP), which is coupled to the hexokinase-G6PD (glucose-6-phosphate dehydrogenase) reaction, generating NADPH (reduced nicotinamide adenine dinucleotide phosphate). The concentration of NADPH is measured by the increase in absorbance at 340/596 nm.

Reaction Equation

$$\text{Creatine Phosphate + ADP} \xrightarrow{\text{CK, } Mg^{2+}} \text{Creatine + ATP}$$

$$\text{D-Glucose + ATP} \xrightarrow{\text{HK, } Mg^{2+}} \text{ADP + G6P}$$

$$\text{G6P + } NADP^{+} \xrightarrow{\text{G6PD}} \text{6-Phosphoglucono-δ-Lactone + NADPH}$$

Reagents

Reagent	Description	Storage	Reagent Stability
REF 10729780	**ADVIA Chemistry Creatine Kinase (CK_L) Reagents**		
Creatine Kinase Reagent 1 CK_L R1	38 mL in 40-mL containers Imidazole buffer (123 mmol/L; pH 6.5) EDTA (2.46 mmol/L) ADP (2.46 mmol/L) AMP (6.14 mmol/L) Diadenosine Pentaphosphate (19 µmol/L) NADP (2.46 mmol/L) HK (≥ 4000 U/L) G-6-PDH (≥ 2800 U/L) N-Acetylcysteine (24.6 mmol/L) Mg^{2+} (12.3 mmol/L)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days
Creatine Kinase Reagent 2 CK_L R2	10 mL in 20-mL containers Buffer (20 mmol/L; pH 8.8) Glucose (120 mmol/L) Creatine Phosphate (184 mmol/L) EDTA (2.46 mmol/L)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

H360D
P201, P202, P280, P281, P308+P313, P501

Danger!
May damage the unborn child.
Obtain special instructions before use. Do not handle until all safety precautions have been read and understood. Wear protective gloves/protective clothing/eye protection/face protection. Use personal protective equipment as required. IF exposed or concerned: Get medical advice/attention. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: Imidazole; ADVIA Chemistry CK_L Reagent 1

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.

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Before use, gently invert the capped reagent to disrupt bubbles and ensure homogeneity. If bubbles still exist or foam is present, use a clean transfer pipette to aspirate them from the reagent container prior to use.

Storing and Stability

Unopened reagents are stable until the expiration date printed on the product label when stored at 2–8°C. Do not freeze reagents.

Specimen Collection and Handling

Siemens Healthcare Diagnostics validated serum (collected using serum separator tubes) and plasma (lithium heparin) for the ADVIA Chemistry CK_L assay.

Follow these guidelines for specimens used for this assay:

- Avoid hemolyzed samples as they may cause significant interference with this assay.
- Serum and plasma can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[3] Follow the instructions provided with your specimen collection device for use and processing.[4]
- Serum samples should have complete clot formation prior to centrifugation.
- Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of 2 hours from the time of collection.[5]
- Specimens should be free of particulate matter.
- Specimens should be as fresh as possible.

The purpose of handling and storage information is to provide guidance to users. 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.

Procedure

Materials Provided

The following materials are provided:

Item	Contents	Number of Tests
REF 10729780	Reagent 1: 4 × 40-mL containers Reagent 2: 4 × 20-mL containers	4 × 275

Materials Required but Not Provided

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

Item	Description
REF 10916059	ADVIA Chemistry Enzyme 3 Calibrator
REF 10316975	20-mL reagent container adapter for 40-mL slot
REF 10723030	20-mL reagent container adapter for 70-mL slot
REF 10719152	40-mL reagent container adapter for 70-mL slot
	Commercially available control materials

Assay Procedure

Sampling, reagent delivery, mixing, and processing are automatically performed by the ADVIA Chemistry XPT system.

For detailed information on performing the procedure, refer to the system operating instructions.

Preparing the System

For detailed information on preparing the system, refer to the system operating instructions.

Preparing the Samples

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles.

On-System Stability

The ADVIA Chemistry CK_L reagents are stable on the system for 30 days.

Do not use reagents beyond the expiration date.

Performing Calibration

To calibrate the ADVIA Chemistry CK_L assay, use the ADVIA Chemistry Enzyme 3 Calibrator, REF 10916059.

The ADVIA Chemistry Enzyme 3 calibrator is a multi-standard calibrator. To set up the calibrator on the system, perform the following steps:

1. Transfer the calibrator to a sample container.
2. Place the sample container that holds the calibrator onto the sample tray (STT) at the cup position assigned to the calibrator.
3. Add water to another sample container and place it at the cup position assigned to the blank for calibration.

Note Multilevel dilution is performed automatically by the ADVIA Chemistry systems using isotonic saline (0.9%).

Enter the lot-specific calibrator values that are provided with each lot of calibrator. Perform the calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay every 30 days.

Calibrate the assay after the following events:

- When the reagent lot number changes
- When a reagent pack is replaced by a new reagent pack with the same lot number, and the previous reagent pack was recalibrated during use
- When a reagent pack is replaced by a new reagent pack with the same lot number, and an additional reagent blank was run on the previous reagent pack during use
- After replacing critical optical or hydraulic components
- When indicated by quality control procedures

Individual laboratory quality control programs and procedures may require more frequent calibration.

Reagent Blank (RBL) Frequency

The ADVIA Chemistry system measures the RBL during assay calibration.

Note Use deionized water as the sample for the RBL in the ADVIA Chemistry CK_L assay.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

At least once each day of use, analyze 2 levels (low and high) of a commercially available quality control (QC) material with known creatine kinase concentrations.

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.

The actual frequency of control in a laboratory is based on many factors, such as workflow, system experience, and government regulation. Each laboratory should evaluate the controls based on the frequency established by their laboratory guidelines.

Also, assay controls under the following conditions:

- Whenever you use a new reagent lot
- Following any system maintenance, cleaning, or troubleshooting procedure
- After performing a new calibration or an additional reagent blank

Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

Taking Corrective Action

If the quality control results do not fall within the expected control range or within the laboratory's established values, do not report results. Take the following actions:

1. Determine and correct the cause of the unacceptable control results:
   a. Verify that the assay was performed according to the instructions for use.
   b. Verify that the materials are not expired.
   c. Verify that required maintenance was performed.
   d. Rerun the assay with fresh quality control samples, and confirm that quality control results are within acceptable limits before running patient samples.
   e. If the quality control results are not within acceptable limits, recalibrate the assay, and repeat the prior step.
   f. If necessary, contact your local technical support provider or distributor for assistance.
2. After corrective action is complete, repeat required testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

The system automatically calculates and reports results based on the absorbance measurements of the test sample during the test, and of the calibrator(s) from calibration.

The instrument calculates the concentration of creatine kinase in U/L (common units or SI units).

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

Avoid hemolyzed samples as they may cause significant interference with this assay.

A number of substances cause physiological changes in serum or plasma analyte concentrations. A comprehensive discussion of possible interfering substances, their serum or plasma concentrations, and their possible physiological involvements is beyond the scope of this document. Consult the listed reference for specific details on known potential interfering substances.[6]

As with any chemical reaction, you must be alert to the possible effect on results of unknown interferences from medications or endogenous substances. The laboratory and physician must evaluate all patient results in light of the total clinical status of the patient.

Expected Values

The reference range for creatine kinase for males is 46–171 U/L. The reference range for creatine kinase for females is 34–145 U/L.[7] Siemens has verified the transference of reported reference ranges for both males and females for the ADVIA Chemistry CK_L assay.[8]

Siemens provides this information for reference. As with all *in vitro* diagnostic assays, each laboratory should determine its own reference ranges for the diagnostic evaluation of patient results. Consider these values as a guideline only.

Performance Characteristics

Analytical Measuring Range

This assay is linear from 15–1300 U/L.

Results that are below the low end of the assay range are flagged **< Conc Range**. You should report the test result as < 15 U/L.

Results that are above the high end of the assay range of 1300 U/L are flagged **> Conc Range**.

Siemens has validated an automatic rerun condition for this assay, samples above 1300 U/L are diluted 1:6 by the system. You may configure the system to trigger automatic reruns. Rerun results will be flagged **Autorepeat.**

Detection Capability

The assay is designed to have the following characteristics:

- A limit of blank (LoB) ≤ 10 U/L
- A limit of detection (LoD) ≤ 15 U/L
- A limit of quantitation (LoQ) ≤ 25 U/L

The LoB, LoD, and LoQ were determined as described in CLSI document EP17-A2.[9]

The LoB is the highest measurement result that is likely to be observed on a blank sample. The LoB for the ADVIA Chemistry CK_L assay is 3 U/L.

The LoD is the smallest amount that this assay can reliably detect to determine presence or absence of an analyte. The LoD for the ADVIA Chemistry CK_L assay is 6 U/L.

The LoB and LoD values are determined with proportions of false positives (α) less than 5% and false negatives (β) less than 5%, based on 450 determinations with 225 blank and 225 low-level sample replicates.

The LoQ is the lowest amount of creatine kinase that can be determined quantitatively within a defined total error. The LoQ for the ADVIA Chemistry CK_L assay is 15 U/L.

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

Precision

The Repeatability precision of the ADVIA Chemistry CK_L assay is designed to have the following characteristics:

- ≤ 4.5% at 30–212 U/L
- ≤ 2.0% at 213–1300 U/L

The Within-Lab precision of the ADVIA Chemistry CK_L assay is designed to have the following characteristics:

- ≤ 6.5% at 30–212 U/L
- ≤ 4.0% at 213–1300 U/L

Each sample was assayed 2 times per run, 2 runs per day, for at least 20 days. The precision of the assay was analyzed as described in CLSI document EP05-A2.[10]

Specimen Type	N	Mean (U/L)	Repeatability (Within-Run) SD[a] (U/L)	Repeatability (Within-Run) CV[b] (%)	Within-Lab (Total) SD[a] (U/L)	Within-Lab (Total) CV[b] (%)
Serum Control 1	80	76	1.6	2.1	2.2	2.9
Serum Control 2	80	233	2.1	0.9	3.5	1.5
Serum Control 3	80	638	3.5	0.6	8.0	1.3
Plasma Pool 1	80	1199	4.8	0.4	6.2	0.5
Serum Pool 1	80	85	2.1	2.4	3.7	4.3
Serum Pool 2	80	194	3.4	1.7	3.4	1.7
Serum Pool 3	80	936	4.3	0.5	5.2	0.6

[a] SD = standard deviation

[b] CV = coefficient of variation

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

Accuracy / Method Comparison

The performance of the ADVIA Chemistry CK_L assay on the ADVIA Chemistry 1800 system (y) was compared with the performance of the comparison assay (x).[11]

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sample Range
Serum	IFCC Reference Method	100	1.00	y = 1.05x - 6.9 U/L	16–1245 U/L
Serum	ADVIA Chemistry CKNAC assay on the ADVIA Chemistry 1800 system	116	1.00	y = 1.01x - 1.8 U/L	22–1280 U/L

The performance of the ADVIA Chemistry CK_L assay on the ADVIA Chemistry 1800 system (x) was compared with the performance of the assay on the indicated system (y).[11]

Specimen Type	Comparison System (y)	N	r	Regression Equation	Sample Range
Serum	ADVIA Chemistry CK_L assay on the ADVIA Chemistry 2400 system	116	1.00	y = 0.97x + 0.9 U/L	24–1230 U/L
Serum	ADVIA Chemistry CK_L assay on the ADVIA Chemistry XPT system	116	1.00	y = 0.98x - 1.9 U/L	22–1242 U/L

The correlation of the assay may vary depending on the study design, comparable method, and sample population. Results obtained at individual laboratories may vary from the data provided.

Matrix Comparison

To confirm the equivalency of sample types, the performance of the ADVIA Chemistry CK_L assay was compared for serum and lithium heparin plasma samples. Testing was performed using one lot of reagents and a single replicate from a matched set of serum and plasma samples in accordance with CLSI document EP09-A3.[11]

Specimen Type (x)	Comparison Specimen (y)	N	r	Regression Equation	Sample Range
Serum	Plasma (lithium heparin)	55	1.00	y = 1.02x - 2.1 U/L	33–1265 U/L

The correlation of the sample types may vary depending on the study design and sample population. Results obtained at individual laboratories may vary from the data provided.

Interferences

Siemens tested the following potential interferents and found the results shown below.[12]

Interferent	Interferent Level	Creatine Kinase Sample Concentration	Interference
Bilirubin (conjugated)	60 mg/dL (1026 µmol/L)	90 U/L	NSI[a]
	60 mg/dL (1026 µmol/L)	257 U/L	NSI
Bilirubin (unconjugated)	60 mg/dL (1026 µmol/L)	93 U/L	NSI
	60 mg/dL (1026 µmol/L)	264 U/L	NSI
Hemolysis (hemoglobin)	125 mg/dL (1.25 g/L)	97 U/L	NSI
	125 mg/dL (1.25 g/L)	278 U/L	NSI
Lipemia (triglycerides from Intralipid)	1000 mg/dL (11.3 mmol/L)	96 U/L	NSI
	1000 mg/dL (11.3 mmol/L)	268 U/L	NSI
Ascorbic Acid	6 mg/dL (341 µmol/L)	86 U/L	NSI
	6 mg/dL (341 µmol/L)	269 U/L	NSI
Sulfasalazine	300 mg/L (753 µmol/L)	92 U/L	NSI
	300 mg/L (753 µmol/L)	262 U/L	NSI
Sulfapyridine	300 mg/L (1.2 mmol/L)	93 U/L	NSI
	300 mg/L (1.2 mmol/L)	262 U/L	NSI

[a] NSI = No significant interference. A percentage effect > 10% is considered a significant interference.

Actual results will vary depending on the study design, the levels of the potential interferences tested, and the samples used. Results obtained at individual laboratories may vary from the data provided.

Standardization

The ADVIA Chemistry CK_L assay is traceable to the IFCC reference method. Refer to the correlation data in the *Accuracy / Method Comparison* section for the relationship.

Technical Assistance

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

siemens.com/healthcare

References

1. Recommendations of the German Society for Clinical Chemistry Standard Method for the Determination of Creatine Kinase Activity Revised Draft of 1976. *J Clin Chem Clin Biochem*. 1977;15:255–260.
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3. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Guideline—Sixth Edition.* CLSI document GP41-A6. Wayne, PA: Clinical and Laboratory Standards Institute; 2007.
4. Clinical and Laboratory Standards Institute (formerly NCCLS). *Tubes and Additives for Venous Blood Specimen Collection: Approved Standard; Approved Guideline—Sixth Edition.* CLSI document GP39-A6. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
5. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Handling and Processing of Blood Specimens; Approved Guideline—Fourth Edition.* CLSI document GP44-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
6. Young DS. *Effects of Drugs on Clinical Laboratory Tests.* 3rd ed. Washington: AACC Press (1990).
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10. Clinical and Laboratory Standards Institute (formerly NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition.* CLSI document EP05-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2004.
11. Clinical and Laboratory Standards Institute (formerly NCCLS). *Measurement Procedure Comparison and Bias Estimation Using Patient Samples—Third Edition.* CLSI document EP09-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.
12. Clinical and Laboratory Standards Institute (formerly NCCLS). *Interference Testing in Clinical Chemistry; Approved Guideline–Second Edition.* CLSI document EP07-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2005.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Keep away from sunlight and heat		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Do not freeze (> 0°C)		Up
	Use by	Σ (n)	Contains sufficient for (n) tests
	Recycle	PRINTED WITH SOY INK	Printed with soy ink
Rev.	Revision	YYYY-MM-DD	Date format (year-month-day)
LOT	Batch code	**RxOnly**	Prescription Device (US only)

Trademarks

Made in: UK

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