SIEMENS Healthineers

Creatine Kinase (CK_L)

Current Revision and Date[a]	Rev. 03, 2019-09	
Product Name	Atellica CH Creatine Kinase (CK_L)	REF 11097640 (996 tests)
Abbreviated Product Name	Atellica CH CK_L	
Test Name/ID	CK_L	
Systems	Atellica CH Analyzer	
Materials Required but Not Provided	Atellica CH ENZ 3 CAL	REF 11099319
Specimen Types	Serum, lithium heparin plasma	
Measuring Interval	Serum: 15–1300 U/L Plasma 15–1300 U/L	

[a] A vertical bar in the page margin indicates technical content that differs from the previous version.

CE

Intended Use

The Atellica® CH 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 the Atellica® CH Analyzer. The assay can be used to aid in the diagnosis and treatment of myocardial infarction and muscle diseases, such as Duchenne progressive muscular dystrophy.

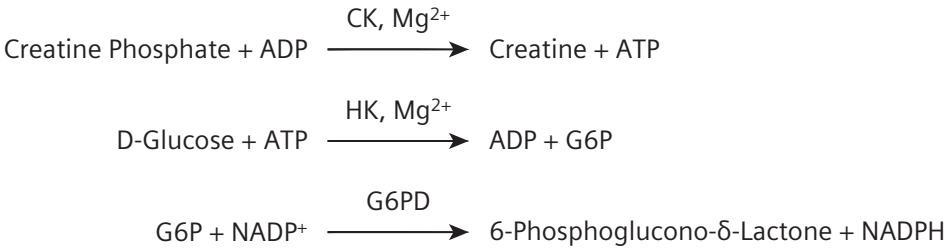
Summary and Explanation

The Atellica CH 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



Reagents

Material Description	Storage	Stability[a]
Atellica CH CK_L	Unopened at 2–8°C	Until expiration date on product
Pack 1 (P1)	Onboard	29 days
Well 1 (W1) Reagent 1 (R1) 23 mL 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) Sodium Azide (0.09%)		
Well 2 (W2) Reagent 1 (R1) 23 mL 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) Sodium Azide (0.09%)		
Pack 2 (P2)		
Well 1 (W1) Reagent 2 (R2) 6 mL Buffer (20 mmol/L; pH 8.8) Glucose (120 mmol/L) Creatine Phosphate (184 mmol/L) EDTA (2.46 mmol/L) Sodium Azide (0.09%)		
Well 2 (W2) Reagent 2 (R2) 6 mL Buffer (20 mmol/L; pH 8.8) Glucose (120 mmol/L) Creatine Phosphate (184 mmol/L) EDTA (2.46 mmol/L) Sodium Azide (0.09%)		

[a] Refer to *Storage and Stability*.

Warnings and Precautions

For *in vitro* diagnostic use.

For Professional Use.

CAUTION

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

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

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

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

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.

Note For information about reagent preparation, refer to *Preparing the Reagents* in the *Procedure* section.

Storage and Stability

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

Do not use products beyond the expiration date printed on the product labeling.

Onboard Stability

Reagents are stable onboard the system for 29 days. Discard reagents at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

Specimen Collection and Handling

Serum and plasma (lithium heparin) are the recommended sample types for this assay.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[3]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[4]
- Follow the instructions provided with your specimen collection device for use and processing.[5]

- Allow blood specimens to clot completely before centrifugation.[6]
- Keep tubes capped at all times.[6]

Storing the Specimen

Specimens may be stored for up to 4 hours at 25°C or for up to 5 days at 2–8°C or stored frozen for up to 2 months at -20°C.[7]

The handling and storage information provided here is based on data or references maintained by the manufacturer. 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.

Transporting the Specimen

Package and label specimens for shipment in compliance with applicable federal and international regulations covering the transport of clinical specimens and etiological agents.

Preparing the Samples

The serum/plasma sample is diluted 1:5 with Atellica CH Diluent (50 µL sample to 200 µL diluent). The Atellica CK_L assay requires 4.5 µL of the diluted sample for a single determination. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. For information about determining the minimum required volume, refer to the online help.

Note Do not use specimens with apparent contamination.

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

Note 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.[6]

Note Specimens should be free of particulate matter.

Before placing samples on the system, ensure that samples are free of:

- Bubbles or foam.
- Fibrin or other particulate matter.

Note For a complete list of appropriate sample containers, refer to the online help.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11097640	**Pack 1 (P1)** Well 1 (W1) 23 mL of Atellica CH CK_L Reagent 1 Well 2 (W2) 23 mL of Atellica CH CK_L Reagent 1 **Pack 2 (P2)** Well 1 (W1) 6 mL of Atellica CH CK_L Reagent 2 Well 2 (W2) 6 mL of Atellica CH CK_L Reagent 2	3 x 332

Materials Required but Not Provided

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

REF	Description	
	Atellica CH Analyzer[a]	
11099319	Atellica CH ENZ 3 CAL (calibrator)	6 x 2.0 mL calibrator CAL Calibrator lot-specific value sheet CAL LOT VAL
	Commercially available quality control materials	

[a] Additional system fluids are required to operate the system: Atellica CH Diluent, Atellica CH Wash, Atellica CH Conditioner, Atellica CH Cleaner, Atellica CH Reagent Probe Cleaner 1, Atellica CH Reagent Probe Cleaner 2, Atellica CH Reagent Probe Cleaner 4, Atellica CH Lamp Coolant, and Atellica CH Water Bath Additive. For system fluid instructions for use, refer to the Document Library.

Assay Procedure

The system automatically performs the following steps:

1. For serum/plasma, dispenses 50 µL of primary sample and 200 µL of Atellica CH Diluent into a dilution cuvette.
2. Dispenses 80 µL of Reagent 1 into a reaction cuvette.
3. Dispenses 4.5 µL of pre-diluted sample into a reaction cuvette.
4. Dispenses 16 µL of Reagent 2 into a reaction cuvette.
5. Mixes and incubates the mixture at 37°C.
6. Measures the absorbance after Reagent 2 addition.
7. Reports results.

Test Duration: 10 minutes

Preparing the Reagents

All reagents are liquid and ready to use.

Preparing the System

Ensure that the system has sufficient reagent packs loaded in the reagent compartment. For information about loading reagent packs, refer to the online help.

Performing Calibration

For calibration of the Atellica CH CK_L assay, use Atellica CH ENZ 3 CAL. Use the calibrators in accordance with the calibrator instructions for use.

Calibration Frequency

Perform a calibration if one or more of the following conditions exist:

- When changing lot numbers of primary reagent packs.
- At the end of the lot calibration interval, for a specified lot of calibrated reagent on the system.
- At the end of the pack calibration interval, for calibrated reagent packs on the system.
- When indicated by quality control results.
- After major maintenance or service.

At the end of the onboard stability interval, replace the reagent pack on the system with a new reagent pack. Recalibration is not required, unless the lot calibration interval is exceeded.

Stability Interval	Days
Lot Calibration	202
Pack Calibration	21
Reagent Onboard Stability	29

For information about lot calibration and pack calibration intervals, refer to the online help.

Follow government regulations or accreditation requirements for calibration frequency. Individual laboratory quality control programs and procedures may require more frequent calibration.

Performing Quality Control

For quality control of the Atellica CH CK_L assay, use at least two levels (low and high) of the appropriate quality control material of known analyte concentration. Use the quality control material in accordance with the quality control instructions for use.

For the assigned values, refer to the lot-specific value sheet provided. 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. Follow your laboratory's quality control procedures if the results obtained do not fall within the acceptable limits. For information about entering quality control definitions, refer to the online help.

Follow government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs and procedures may require more frequent quality control testing.

Taking Corrective Action

If the quality control results do not fall within the assigned values, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the online help.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the online help. The system reports results in U/L (common units).

For information about results outside the specified measuring interval, refer to *Measuring Interval*.

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

The Atellica CH CK_L assay is limited to the detection of creatine kinase in human serum and plasma (lithium heparin).

Do not use 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.[8]

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

Reference Interval

The reference interval for creatine kinase for males is 46–171 U/L. The reference interval for creatine kinase for females is 34–145 U/L.[9]

A reference interval confirmed in accordance with CLSI Document EP28-A3c on the Atellica CH Analyzer.[10],[11]

Group	Reference Interval
Adult males	46–171 U/L
Adult females	34–145 U/L

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results. Consider these values as guidance only.[10]

Performance Characteristics

Measuring Interval

The Atellica CH CK_L assay provides results from 15 U/L to 1300 U/L. The system flags all values that are outside the specified measuring interval.

Extended Measuring Interval

An automatic repeat condition for this assay extends the measuring interval to 7800 U/L for serum and plasma. You may configure the system to trigger an automatic repeat. Automatic repeat results will be flagged **Autorepeat**.

Detection Capability

Detection capability was determined in accordance with CLSI Document EP17-A2.[12] The assay is designed to have a limit of blank (LoB) ≤ 10 U/L, a limit of detection (LoD) ≤ 15 U/L, and a limit of quantitation (LoQ) ≤ 25 U/L.

The LoD corresponds to the lowest concentration of creatine kinase that can be detected with a probability of 95%. The LoD for the Atellica CH CK_L assay is 6 U/L, and was determined using 225 determinations, with 75 blank and 75 low level replicates, and a LoB of 1 U/L .

The LoQ corresponds to the lowest amount of analyte in a sample at which the total error is ≤ 10 U/L. The LoQ of the Atellica CH CK_L assay is 6 U/L, and was determined using multiple patient samples in the interval 6–16 U/L. All samples were assayed in replicates of 5 using 3 reagent lots, over a period of 5 days.

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[13] Samples were assayed on an Atellica CH Analyzer in duplicate in 2 runs per day for 20 days (N ≥ 80 for each sample). The following results were obtained:

			Repeatability		Within-Lab Precision	
Sample Type	**N**	**Mean U/L**	**SD[a] U/L**	**CV[b] (%)**	**SD U/L**	**CV (%)**
Serum Pool 1	80	962	4.0	0.4	6.5	0.7
Serum Pool 2	80	1152	3.4	0.3	7.8	0.7
Plasma Pool	80	198	1.5	0.8	2.1	1.1
QC 1	80	84	1.3	1.6	2.0	2.4
QC 2	80	258	3.1	1.2	4.2	1.6
QC 3	80	640	2.4	0.4	7.4	1.2

[a] Standard deviation.
[b] Coefficient of variation.

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

Assay Comparison

The Atellica CH CK_L assay is designed to have a correlation coefficient of ≥ 95% and a slope of 1.0 ± 0.1 compared to ADVIA Chemistry CK_L. Assay comparison was determined using the Deming linear regression model in accordance with CLSI Document EP09-A3.[14] The following results were obtained:

Specimen	**Comparative Assay (x)**	**Regression Equation**	**Sample Interval**	**N[a]**	**r[b]**
Serum	ADVIA Chemistry CK_L	y = 0.96x + 3.1 U/L	17–1289 U/L	177	1.00

[a] Number of samples tested.
[b] Correlation coefficient.

The agreement of the assay may vary depending on the study design, comparative assay, and sample population. Assay results obtained at individual laboratories may vary from the data presented.

Specimen Equivalency

Specimen equivalency was determined using the Deming linear regression model in accordance with CLSI Document EP09-A3.[14] The following results were obtained:

Specimen (y)	**Reference Specimen (x)**	**Regression Equation**	**Sample Interval**	**N[a]**	**r[b]**
Lithium heparin	Serum	y = 0.99x - 0.3 U/L	57–1062 U/L	57	1.00

[a] Number of samples tested.
[b] Correlation coefficient.

Agreement of the specimen types may vary depending on the study design and sample population used. Assay results obtained at individual laboratories may vary from the data presented.

Interferences

Hemolysis, Icterus, and Lipemia (HIL)

The Atellica CH CK_L assay is designed to have ≤ 10% interference from hemoglobin, bilirubin, and lipemia. Interfering substances at the levels indicated in the table below were tested in accordance with CLSI Document EP07-A2 using the Atellica CH CK_L assay.[15]

Bias is the difference in the results between the control sample (does not contain the interferent) and the test sample (contains the interferent) expressed in percent. Bias > 10% is considered interference. Analyte results should not be corrected based on this bias.

Substance	Substance Test Concentration	Analyte Concentration	Percent Bias
Hemoglobin	125 mg/dL (1.25 g/L)	100 U/L	10%
	125 mg/dL (1.25 g/L)	289 U/L	3%
Bilirubin, conjugated	60 mg/dL (1026 µmol/L)	85 U/L	0%
	60 mg/dL (1026 µmol/L)	242 U/L	0%
Bilirubin, unconjugated	60 mg/dL (1026 µmol/L)	87 U/L	-3%
	60 mg/dL (1026 µmol/L)	247 U/L	-2%
Lipemia (Intralipid®)	1000 mg/dL (11.3 mmol/L)	97 U/L	4%
	1000 mg/dL (11.3 mmol/L)	285 U/L	-1%

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

Non-Interfering Substances

The following substances do not interfere with the Atellica CH CK_L assay when present in serum and plasma at the concentrations indicated in the table below. Bias due to these substances is ≤ 10% at analyte concentrations indicated in the table below. These data were generated on the ADVIA Chemistry 1800 system with assay reaction conditions that are equivalent to those on the Atellica CH Analyzer.[11]

Substance	Substance Test Concentration Common Units (SI Units)	Analyte Concentration	Percent Bias
Ascorbic Acid	6 mg/dL (341 µmol/L)	91 U/L	4%
	6 mg/dL (341 µmol/L)	271 U/L	1%
Sulfasalazine	300 mg/L (753 µmol/L)	94 U/L	0%
	300 mg/L (753 µmol/L)	264 U/L	2%

Substance	Substance Test Concentration Common Units (SI Units)	Analyte Concentration	Percent Bias
Sulfapyridine	300 mg/L (1.2 mmol/L)	93 U/L	1%
	300 mg/L (1.2 mmol/L)	263 U/L	2%

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

Standardization

The Atellica CH CK_L assay is traceable to the IFCC reference method. Assigned values for calibrators are traceable to this standardization.[11]

Technical Assistance

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

siemens.com/healthineers

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.
2. Szasz G, Gruber W, Bernt E. Creatine kinase in serum: Determination of optimum reaction conditions. *Clin Chem*. 1976;22:650–656.
3. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document M29-A4.
4. Clinical and Laboratory Standards Institute. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2007. CLSI Document GP41-A6.
5. Clinical and Laboratory Standards Institute. *Tubes and Additives for Venous and Capillary Blood Specimen Collection; Approved Standard—Sixth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP39-A6.
6. Clinical and Laboratory Standards Institute. *Procedures for the Handling and Processing of Blood Specimens for Common Laboratory Tests; Approved Guideline—Fourth Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document GP44-A4.
7. Wu AHB, ed. *Tietz Clinical Guide to Laboratory Tests,* 4th ed. St. Louis, MO: WB Saunders Company; 2006:306.
8. Young DS. *Effects of Drugs on Clinical Laboratory Tests*. 5th ed. Washington, DC: AACC Press; 2000.
9. Burtis CA, Ashwood ER, and Bruns DE. *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*. 5th ed. St. Louis, MO: Saunders Elsevier; 2012.
10. Clinical and Laboratory Standards Institute. *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2010. CLSI Document EP28-A3c.
11. Data on file at Siemens Healthcare Diagnostics.
12. Clinical and Laboratory Standards Institute. *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2012. CLSI Document EP17-A2.

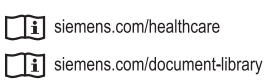
13. Clinical and Laboratory Standards Institute. *Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2014. CLSI Document EP05-A3.

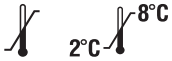
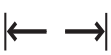
14. Clinical and Laboratory Standards Institute. *Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013. CLSI Document EP09-A3.

15. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2005. CLSI Document EP07-A2.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
	Version of instructions for use
	Internet URL address to access the electronic instructions for use
	Revision
	Caution Consult instructions for use or accompanying documents for cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the medical device.
	Biological risks Potential biological risks are associated with the medical device.
	Corrosive
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing

Symbol	Symbol Title and Description
	Explosive
	Toxic
	Compressed gas
	Keep away from sunlight Prevent exposure to sunlight and heat.
	Up Store in an upright position.
	Do not freeze
	Temperature limit Upper and lower limits of temperature indicators are adjacent to the upper and lower horizontal lines.
	Handheld barcode scanner
	*In vitro* diagnostic medical device
	Contains sufficient for <n> tests Total number of IVD tests the system can perform with the IVD kit reagents appears adjacent to the symbol.
RxOnly	Prescription device (US only) Applies only to United States-registered IVD assays. CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.
	Mixing of substances Mix product before use.
	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
	Authorized Representative in the European Community
	Use-by date Use by the designated date.

Symbol	Symbol Title and Description
LOT	Batch code
REF	Catalog number
	Recycle
	Printed with soy ink
CE	CE Mark
CE 0088	CE Mark with notified body ID number Notified body ID number can vary.
YYYY-MM-DD	Date format (year-month-day)
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
UNITS C	Common Units
UNITS SI	International System of Units
MATERIAL	Material
MATERIAL ID	Unique material identification number
CONTROL NAME	Name of control
CONTROL TYPE	Type of control

Legal Information

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