SIEMENS Healthineers

Enzymatic Creatinine_3 (ECre3)

Current Revision and Date[a]	Rev. 03, 2022-06	
Product Name	Atellica CH Enzymatic Creatinine_3 (ECre3)	REF 11537216 (2000 tests)
Abbreviated Product Name	Atellica CH ECre3	
Test Name/ID	ECre3	
Systems	Atellica CH Analyzer	
Materials Required but Not Provided	Atellica CH CHEM CAL	REF 11099411
Specimen Types	Serum, lithium heparin plasma, dipotassium EDTA plasma, urine	
Sample Volume	8.5 µL	
Measuring Interval	Serum/plasma: 0.15–30.00 mg/dL (13–2652 µmol/L) Urine: 2.00–245.00 mg/dL (177–21,658 µmol/L)	

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

CE

Intended Use

The Atellica® CH Enzymatic Creatinine_3 (ECre3) assay is for *in vitro* diagnostic use in the quantitative determination of creatinine in human serum, plasma (lithium heparin and dipotassium EDTA), and urine using the Atellica® CH Analyzer. Such measurements are used in the diagnosis and treatment of renal diseases and in monitoring renal dialysis.

Summary and Explanation

The Atellica CH ECre3 assay measures the concentration of creatinine through a series of coupled enzymatic reactions and is based upon the method developed by Suzuki and Yoshida.[1]

Principles of the Procedure

The Atellica CH ECre3 assay uses a series of coupled enzymatic reactions. In a "pretreatment" reaction, endogenous creatine and sarcosine are removed from a test sample by creatinase and sarcosine oxidase. The level of creatinine in a test sample is then determined through coupled enzymatic reactions. First, creatinine is enzymatically converted by creatininase into creatine. Creatine is then enzymatically converted to sarcosine by creatinase. This is followed by the oxidation of sarcosine by sarcosine oxidase to produce hydrogen peroxide. In the presence of peroxidase, the hydrogen peroxide allows for the oxidative condensation of 4-aminoantipyrine and N-ethyl-N-(3-methylphenyl)-N'-succinyl-ethylenediamine to produce a reddish purple quinone pigment. The absorbance of this quinone pigment is measured as an endpoint reaction at 545/694 nm.

Reagents

Material Description	Storage	Stability[a]
Atellica CH ECre3	Unopened at 2–8°C	Until expiration date on product
Pack 1 (P1)	Onboard per well	90 days
Well 1 (W1) and Well 2 (W2) Reagent 1 (R1) 23.5 mL Creatinase (< 133,350 U/L); sarcosine oxidase (< 39,000 U/L); N-ethyl-N-(3-methylphenyl)-N′-succinyl-ethylenediamine (EMSE) (0.04%); detergent; preservatives; bovine serum albumin (0.1%); bovine catalase (< 180,000 U/L)		
Pack 2 (P2)		
Well 1 (W1) and Well 2 (W2) Reagent 2 (R2) 11.5 mL Peroxidase (< 36,000 U/L); creatininase (< 600,000 U/L); 4-aminoantipyrine (4-AA) (0.07%); detergent; sodium azide (< 0.1%); preservatives		

[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-healthineers.com.

CAUTION

This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

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.

Storage and Stability

Store reagents away from light. Do not use products beyond the expiration date printed on the product labeling.

For details about product material description, storage, and stability, refer to *Reagents*.

Onboard Stability

Discard products at the end of the onboard stability interval.

For details about product onboard stability, refer to *Reagents*.

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

Note Refer to the supplementary document "Atellica Sample Handler Calibrator and QC Storage and Stability" for information about storage and stability of materials in the Cal-QC tube storage area.

Specimen Collection and Handling

Serum, lithium heparin plasma, dipotassium EDTA plasma, and urine are the recommended specimen types for this assay.

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.

Collecting the Specimen

- Observe universal precautions when collecting specimens. Handle all specimens as if they are capable of transmitting disease.[2]
- Follow 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]
- Specimens with high turbidity or particulates should be centrifuged before analysis.
- Allow blood specimens to clot completely before centrifugation.[5]
- Keep tubes capped at all times.[5]
- Urine specimens may be collected in glass or plastic (such as polypropylene, polycarbonate, or polyethylene) containers.
- Collect urine as a 24-hour, timed, or random midstream sample (spot collection) in a clean, unused glass or plastic collection container.
- Random urine specimens may be used but timed 24-hr specimens are preferred. No preservative is required during 24-hour collection.
- Urine specimens must be free of particulate matter before analysis.
- Do not use hemolyzed specimens.
- Adulteration of the urine specimen may cause erroneous results. If adulteration is suspected, obtain another specimen.

Storing the Specimen

Specimen Type(s)	Storage Condition(s)	Storage Duration
Serum/plasma	18–26°C[6]	48 hours
	2–8°C[6]	8 days
	Frozen at -20°C[6]	37 days
Urine	2–8°C[6]	8 days
	Frozen at -20°C[6]	37 days

For specimens that are frozen:

- Do not store in a frost-free freezer.

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

This assay requires 8.5 µL of serum, lithium heparin plasma, dipotassium EDTA plasma or urine 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 system operating instructions.

Do not use samples with apparent contamination.

Frozen specimens must be thawed and mixed thoroughly prior to analysis.

Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[5]

For a complete list of appropriate sample containers, refer to the system operating instructions.

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

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

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
11537216	Atellica CH ECre3 **Pack1 (P1)** Well 1 (W1) 23.5 mL of Reagent 1 Well 2 (W2) 23.5 mL of Reagent 1 **Pack 2 (P2)** Well 1 (W1) 11.5 mL of Reagent 2 Well 2 (W2) 11.5 mL of Reagent 2	4 x 500

Materials Required but Not Provided

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

REF	Description	
	Atellica CH Analyzer[a]	
11099411	Atellica CH CHEM CAL	12 x 3.0 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.

   For urine, dispenses 12.5 µL of primary sample and 237.5 µL of Atellica CH Diluent into a dilution cuvette.
2. Dispenses 85 µL of Reagent 1 and 5 µL of special reagent water into a reaction cuvette.
3. Dispenses 8.5 µL of pre-diluted sample into a reaction cuvette.
4. Measures the absorbance after sample addition.
5. Dispenses 28.4 µL of Reagent 2 into a reaction cuvette.
6. Mixes and incubates the mixture at 37°C.
7. Measures the absorbance after Reagent 2 addition.
8. Reports results.

Note For information about special reagent water, refer to the system operating instructions.

Test Duration: 10 minutes

Preparing the Reagents

All reagents are liquid and ready to use.

Preparing the System

For information about loading reagents, refer to the system operating instructions.

Performing Calibration

For calibration of the Atellica CH ECre3 assay, use Atellica CH CHEM CAL. Use the calibrators in accordance with the calibrator instructions for use.

Calibration Frequency

Calibration Interval	Days
Lot Calibration	180
Pack Calibration	90

In addition, perform a calibration:

- When changing lot numbers of reagents.
- 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 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.

Note When loading new reagents, recalibration is not required if there is a valid lot calibration. For information about the calibration interval, refer to the system operating instructions.

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

Performing Quality Control

At least once each day of use, analyze two levels of quality control (QC) material with known creatinine concentration. For assistance in identifying a quality control material, refer to the *Atellica CH Quality Control Material Supplement* available on siemens-healthineers.com. Additional quality control material can be used at the discretion of the laboratory. Use the quality control material in accordance with the quality control instructions for use.

In addition, perform quality control:

- Following a valid calibration.
- With use of a new lot of reagent.
- When troubleshooting test results that do not match clinical conditions or symptoms.

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

Acceptable performance is achieved when the analyte values obtained are within the expected control interval for the system, as indicated by the manufacturer of the control material or within the interval determined by an internal laboratory quality control procedure.

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 system operating instructions.

Taking Corrective Action

If the quality control results do not fall within the expected control interval, do not report results. Perform corrective actions in accordance with established laboratory protocol. For suggested protocol, refer to the system operating instructions.

Results

Calculation of Results

The system determines the result using the calculation scheme described in the system operating instructions. The system reports results in mg/dL (conventional units) or µmol/L (SI units [Systèm International d'Unités]), depending on the units defined when setting up the assay.

Conversion formula: mg/dL x 88.4 = µmol/L

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 following information pertains to limitations of the assay:

- The Atellica CH ECre3 assay is limited to the detection of creatinine in serum, lithium heparin plasma, dipotassium EDTA plasma, and urine.
- As with any chemical reaction, you must be alert to the possible effect 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.
- Blood samples from some patients with monoclonal gammopathies may produce falsely elevated results.[7]
- Use of this assay is not recommended for patients being treated with Calcium dobesilate (Dexium). Calcium dobesilate concentrations above 0.38 mg/dL (9.1 µmol/L) may produce falsely depressed results. Calcium dobesilate at 6 mg/dL (143.4 µmol/L) causes a decrease in the analyte concentration by -46.0% at 1.00 mg/dL (88 µmol/L) and -15.3% at 8.67 mg/dL (766 µmol/L).
- Venipuncture should occur prior to N-Acetyl Cysteine (NAC) or Metamizole (Sulpyrine) administration due to the potential for falsely depressed results.
- Use of this assay is not recommended for patients being treated with N-Acetyl Cysteine (NAC). NAC concentrations above 37.5 mg/dL (2.3 mmol/L) may produce falsely depressed results. NAC at 150 mg/dL (9.2 mmol/L) causes a decrease in the analyte concentration by -51.0% at 0.98 mg/dL (87 µmol/L) and -38.7% at 8.40 mg/dL (743 µmol/L).
- Use of this assay is not recommended for patients being treated with Metamizole (Sulpyrine). Metamizole concentrations above 25 mg/dL (750 µmol/L) may produce falsely depressed results. Metamizole at 100 mg/dL (3000 µmol/L) causes a decrease in the analyte concentration by -14.3% at 0.98 mg/dL (87 µmol/L) and -15.3% at 8.48 mg/dL (750 µmol/L).
- Use of this assay is not recommended for patients being treated with N-acetyl-p-benzoquinone imine (NAPQI). NAPQI concentrations above 0.4 mg/dL (26.8 µmol/L) may produce falsely depressed results. NAPQI at 1.5 mg/dL (100.7 µmol/L) causes a decrease in the analyte concentration by -17.6% at 1.02 mg/dL (90 µmol/L) and -4.2% at 8.75 mg/dL (774 µmol/L).

- Use of this assay is not recommended for patients being treated with Methyl dopa. Methyl dopa concentrations above 11.3 µg/mL (53.5 µmol/L) may produce falsely depressed results. Methyl dopa at 22.5 µg/mL (106.5 µmol/L) causes a decrease in the analyte concentration by -14.9% at 1.01 mg/dL (89 µmol/L) and -8.2% at 7.42 mg/dL (656 µmol/L).
- Use of this assay is not recommended for patients being treated with Rifampicin. Rifampicin concentrations above 2.4 mg/dL (29.2 µmol/L) may produce falsely depressed results. Rifampicin at 4.8 mg/dL (58.3 µmol/L) causes a decrease in the analyte concentration by -14.1% at 0.99 mg/dL (88 µmol/L) and -3.7% at 8.47 mg/dL (749 µmol/L).
- Use of this assay is not recommended for patients being treated with Dicynone (etamsylate). Etamsylate concentrations above 0.59 mg/dL (22.4 µmol/L) may produce falsely depressed results. Etamsylate at 5 mg/dL (190 µmol/L) causes a decrease in the analyte concentration by -50.0% at 0.96 mg/dL (85 µmol/L) and -23.4% at 7.79 mg/dL (689 µmol/L).
- Use of this assay is not recommended for patients being treated with phenindione due to the reported falsely depressed results from phenindione metabolites.[8]
- N-ethylglycine (a metabolite of lidocaine) concentrations above 0.4 mg/dL (38.8 µmol/L) may produce falsely elevated results. N-ethylglycine at 6.5 mg/dL (630.3 µmol/L) causes an increase in the analyte concentration by 84.4% at 1.09 mg/dL (96 µmol/L) and 12.9% at 7.83 mg/dL (692 µmol/L).[9]
- A number of substances cause physiological changes in serum, plasma or urine analyte concentrations. A comprehensive discussion of possible interfering substances, their 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.

Expected Values

Reference Interval

Siemens Healthineers has verified the reference interval for serum, plasma and urine for the Atellica CH ECre3 assay, in accordance with CLSI Document EP28-A3c.[10]

Group	Specimen Type	Reference Interval Conventional Units (SI Units)
Males[a]	Serum/plasma[11]	0.73–1.18 mg/dL (65–104 µmol/L)
Females[a]	Serum/plasma[11]	0.55–1.02 mg/dL (49–90 µmol/L)
Males	Urine[12]	800–2000 mg/day
Females	Urine[12]	600–1800 mg/day

[a] These data were verified on the Atellica CH Analyzer.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference interval for the diagnostic evaluation of patient results.[13] Consider these values as guidance only.

Performance Characteristics

Measuring Interval

The Atellica CH ECre3 assay is linear from 0.15 mg/dL (13 µmol/L) to 30.00 mg/dL (2652 µmol/L) for serum and plasma and 2.00 mg/dL (177 µmol/L) to 245.00 mg/dL (21,658 µmol/L) for urine. The system flags all values that are outside the specified measuring interval.

The lower end of the measuring interval is defined by the limit of quantitation (LoQ). Report results below the measuring interval as < 0.15 mg/dL (13 µmol/L) for serum and plasma and < 2.00 mg/dL (177 µmol/L) for urine.

Extended Measuring Interval

An automatic repeat condition for this assay extends the measuring interval to 150.00 mg/dL (13,260 µmol/L) for serum and plasma, and to 1225.00 mg/dL (108,290 µmol/L) for urine. You may configure the system to trigger an automatic repeat. Automatic repeat results will be flagged **Autorepeat**.

Detection Capability

The Limit of Blank (LoB) corresponds to the highest measurement result that is likely to be observed for a blank sample. The assay is designed to have an LoB ≤ Limit of Detection (LoD).

The LoD corresponds to the lowest concentration of creatinine that can be detected with a probability of 95%. The assay is designed to have an LoD ≤ Limit of Quantitation (LoQ).

The LoQ corresponds to the lowest concentration of creatinine in a sample at which the total analytical error is ≤ 0.10 mg/dL for serum and plasma and ≤ 1.50 mg/dL for urine. The assay is designed to have an LoQ ≤ 0.15 mg/dL (13 µmol/L) for serum and plasma and ≤ 2.00 mg/dL (177 µmol/L) for urine.

Detection capability was determined in accordance with CLSI Document EP17-A2.[14]

The study supports the following detection capability claims:

Specimen Type	Detection Capability	mg/dL (µmol/L)
Serum/plasma	LoB	0.05 (4)
	LoD	0.10 (9)
	LoQ	0.15 (13)
Urine	LoB	0.15 (13)
	LoD	0.50 (44)
	LoQ	2.00 (177)

The LoD was determined using 120 determinations, with 60 blank and 60 low-level replicates, and a LoB of 0.05 mg/dL (4 µmol/L) for serum and plasma and 0.15 mg/dL (13 µmol/L) for urine.

The LoQ was determined using multiple patient samples ≤ 0.15 mg/dL (13 µmol/L) for serum and plasma and ≤ 2.00 mg/dL (177 µmol/L) for urine. All samples were assayed n=5 using 3 reagent lots, over a period of 3 days.

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

Precision

The assay is designed to have the following precision:

- Repeatability:
  - Serum/plasma: SD ≤ 0.04 mg/dL at 0.30–0.49 mg/dL
  - Serum/plasma: CV ≤ 3.5% at 0.50–0.99 mg/dL
  - Serum/plasma: CV ≤ 2.0% at 1.00–30.00 mg/dL
  - Urine: CV ≤ 2.0% at 35.00–245.00 mg/dL
- Within-Laboratory:
  - Serum/plasma: SD ≤ 0.05 mg/dL at 0.30–0.49 mg/dL
  - Serum/plasma: CV ≤ 4.0% at 0.50–0.99 mg/dL
  - Serum/plasma: CV ≤ 2.5% at 1.00–30.00 mg/dL
  - Urine: CV ≤ 2.5% at 35.00–245.00 mg/dL

Precision was determined in accordance with CLSI Document EP05-A3.[15] Samples were assayed on the Atellica CH Analyzer in duplicate in 2 runs per day for 20 days.

The following results were obtained:

			Repeatability		Within-Laboratory Precision	
Specimen Type	N[a]	Mean mg/dL (µmol/L)	SD[b] mg/dL (µmol/L)	CV[c] (%)	SD mg/dL (µmol/L)	CV (%)
Serum 1	80	0.41 (36)	0.009 (0.8)	2.2	0.013 (1.1)	3.2
Serum 2	80	0.75 (66)	0.008 (0.7)	1.1	0.015 (1.3)	2.0
Serum 3	80	1.29 (114)	0.010 (0.9)	0.8	0.030 (2.7)	2.3
Serum QC 1	80	1.91 (169)	0.012 (1.1)	0.6	0.024 (2.1)	1.3
Serum QC 2	80	3.11 (275)	0.009 (0.8)	0.3	0.026 (2.3)	0.8
Serum 4	80	8.89 (786)	0.021 (1.9)	0.2	0.055 (4.9)	0.6
Serum 5	80	18.52 (1637)	0.039 (3.4)	0.2	0.093 (8.2)	0.5
Serum 6	80	26.49 (2342)	0.054 (4.8)	0.2	0.121 (10.7)	0.5
Urine 1	80	42.82 (3785)	0.064 (5.7)	0.1	0.322 (28.5)	0.8
Urine QC 1	80	86.41 (7639)	0.156 (13.8)	0.2	0.497 (43.9)	0.6
Urine 2	80	185.06 (16,359)	0.320 (28.3)	0.2	0.831 (73.5)	0.4

[a] Number of results.
[b] Standard deviation.
[c] Coefficient of variation.

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

Reproducibility

The assay is designed to have the following reproducibility:

- Serum/plasma: SD ≤ 0.06 mg/dL at 0.30–0.49 mg/dL
- Serum/plasma: CV ≤ 8.0% at 0.50–0.99 mg/dL

- Serum/plasma: CV ≤ 5.0% at 1.00–30.00 mg/dL
- Urine: CV ≤ 5.0% at 35.00–245.00 mg/dL

Reproducibility was determined in accordance with CLSI Document EP05-A3.[15] Samples were assayed n=5 in 1 run for 5 days using 3 instruments and 3 reagent lots. The data were analyzed to calculate the following components of precision: repeatability, between-day, between-lot, between-instrument, and reproducibility (total). The following results were obtained:

			Repeatability		Between-Day		Between-Lot		Between-Instrument		Total Reproducibility	
Sample	N[a]	Mean mg/dL (µmol/L)	SD[b] mg/dL (µmol/L)	CV[c] (%)	SD mg/dL (µmol/L)	CV (%)	SD mg/dL (µmol/L)	CV (%)	SD mg/dL (µmol/L)	CV (%)	SD mg/dL (µmol/L)	CV (%)
Serum 1	225	0.44 (39)	0.008 (0.8)	1.9	0.005 (0.4)	1.1	0.008 (0.7)	1.9	0.000 (0.0)	0.0	0.013 (1.1)	2.9
Serum QC 1	225	0.79 (70)	0.011 (0.9)	1.3	0.004 (0.3)	0.5	0.008 (0.7)	1.0	0.000 (0.0)	0.0	0.014 (1.2)	1.7
Serum 2	225	0.95 (84)	0.014 (1.2)	1.4	0.034 (3.0)	3.5	0.000 (0.0)	0.0	0.007 (0.6)	0.7	0.037 (3.3)	3.9
Serum QC 2	225	1.88 (166)	0.011 (1.0)	0.6	0.008 (0.7)	0.4	0.009 (0.8)	0.5	0.000 (0.0)	0.0	0.016 (1.4)	0.8
Serum QC 3	225	6.82 (603)	0.016 (1.4)	0.2	0.022 (1.9)	0.3	0.000 (0.0)	0.0	0.017 (1.5)	0.2	0.032 (2.8)	0.5
Serum 3	225	7.96 (703)	0.021 (1.8)	0.3	0.034 (3.0)	0.4	0.000 (0.0)	0.0	0.019 (1.7)	0.2	0.045 (3.9)	0.6
Serum 4	225	26.86 (2374)	0.051 (4.5)	0.2	0.105 (9.3)	0.4	0.039 (3.5)	0.1	0.082 (7.2)	0.3	0.148 (13.1)	0.6
Urine 1	225	42.30 (3739)	0.106 (9.3)	0.2	0.102 (9.0)	0.2	0.000 (0.0)	0.0	0.171 (15.1)	0.4	0.225 (19.9)	0.5
Urine 2	225	189.56 (16,757)	0.379 (33.5)	0.2	0.401 (35.4)	0.2	0.503 (44.5)	0.3	1.024 (90.5)	0.5	1.267 (112.0)	0.7

[a] Number of results.
[b] Standard deviation.
[c] Coefficient of variation.

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

Assay Comparison

The Atellica CH ECre3 assay (y) was designed to have a correlation coefficient of ≥ 0.950 and a slope of 1.00 ± 0.05 compared to the ADVIA Chemistry ECRE_2 assay. Assay comparison for serum was determined using the Deming regression model and for urine using the Weighted Deming regression model in accordance with CLSI Document EP09c.[16] The following results were obtained:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ADVIA Chemistry 1800 ECRE_2	y = 0.99x + 0.02 mg/dL (y = 0.99x + 2 µmol/L)	0.18–28.41 mg/dL (16–2511 µmol/L)	105	1.000
Urine	ADVIA Chemistry 1800 ECRE_2	y = 0.98x + 0.05 mg/dL (y = 0.98x + 4 µmol/L)	4.71–240.47 mg/dL (416–21,258 µmol/L)	102	0.999
Serum/plasma	Isotope Dilution Mass Spectrometry (IDMS)	y = 1.01x + 0.01 mg/dL (y = 1.01x + 1 µmol/L)	0.35–26.70 mg/dL (31–2360 µmol/L)	47	0.991

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

Agreement of the assays 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 regression model in accordance with CLSI Document EP09c.[16] The following results were obtained:

Specimen (y)	Reference Specimen (x)	Regression Equation	Sample Interval	N[a]	r[b]
Lithium heparin plasma	Serum	y = 0.99x + 0.00 mg/dL (y = 0.99x + 0 µmol/L)	0.50–26.91 mg/dL (44–2379 µmol/L)	55	1.000
Dipotassium EDTA plasma	Serum	y = 0.97x + 0.02 mg/dL (y = 0.97x + 2 µmol/L)	0.50–26.91 mg/dL (44–2379 µmol/L)	55	0.998

[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)

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. The Atellica CH ECre3 assay is designed to have ≤ 10% interference from hemoglobin, bilirubin, and lipemia. Bias > 10% is considered interference. Analyte results should not be corrected based on this bias.

Interference testing was performed in accordance with CLSI Document EP07.[17] The following results were obtained:

Substance	Substance Concentration Conventional Units (SI Units)	Analyte Concentration Conventional Units (SI Units)	Bias %
Hemoglobin	200 mg/dL (2.0 g/L) 1000 mg/dL (10.0 g/L)	1.00 mg/dL (88 µmol/L) 8.25 mg/dL (729 µmol/L)	6.0 -3.2
Bilirubin, conjugated	25 mg/dL (427.5 µmol/L) 25 mg/dL (427.5 µmol/L)	0.97 mg/dL (86 µmol/L) 8.76 mg/dL (774 µmol/L)	-6.2 -3.1

Substance	Substance Concentration Conventional Units (SI Units)	Analyte Concentration Conventional Units (SI Units)	Bias %
Bilirubin, unconjugated	25 mg/dL (427.5 µmol/L) 25 mg/dL (427.5 µmol/L)	0.97 mg/dL (86 µmol/L) 8.66 mg/dL (766 µmol/L)	-4.1 -1.6
Lipemia (Intralipid®)	2000 mg/dL (20.0 g/L) 2000 mg/dL (20.0 g/L)	1.06 mg/dL (94 µmol/L) 8.06 mg/dL (713 µmol/L)	-3.8 -2.6

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 ECre3 assay when present in serum, lithium heparin plasma, dipotassium EDTA plasma, and urine at the concentrations indicated in the tables below. Bias due to these substances is ≤ 10% at an analyte concentration of 1.00 mg/dL and 8.00 mg/dL for serum and 40.00 mg/dL and 180.00 mg/dL for urine.

Serum

Substance	Highest Concentration Tested with No Interference Conventional Units (SI Units)	Analyte Concentration Conventional Units (SI Units)	%
Acetaminophen	200 µg/mL (1.3 mmol/L) 200 µg/mL (1.3 mmol/L)	0.94 mg/dL (83 µmol/L) 8.32 mg/dL (735 µmol/L)	1.1 -0.2
Calcium dobesilate (Dexium)	0.38 mg/dL (9.1 µmol/L) 0.38 mg/dL (9.1 µmol/L)	1.02 mg/dL (90 µmol/L) 8.74 mg/dL (773 µmol/L)	-6.9 -2.1
Cefoxitin	6600 µg/mL (15.4 mmol/L) 6600 µg/mL (15.4 mmol/L)	1.04 mg/dL (92 µmol/L) 7.44 mg/dL (658 µmol/L)	-8.7 -1.1
Cephalexin	200 µg/mL (575.7 µmol/L) 200 µg/mL (575.7 µmol/L)	0.92 mg/dL (81 µmol/L) 7.90 mg/dL (698 µmol/L)	1.1 -0.4
Dicynone (Etamsylate)	0.59 mg/dL (22.4 µmol/L) 0.59 mg/dL (22.4 µmol/L)	1.01 mg/dL (89 µmol/L) 8.64 mg/dL (764 µmol/L)	-8.9 -2.1
DL-proline	11.5 mg/dL (998.9 µmol/L) 11.5 mg/dL (998.9 µmol/L)	0.98 mg/dL (87 µmol/L) 8.49 mg/dL (751 µmol/L)	3.1 0.2
Dobutamine	5 µg/mL (16.6 µmol/L) 5 µg/mL (16.6 µmol/L)	0.98 mg/dL (87 µmol/L) 8.62 mg/dL (762 µmol/L)	-5.1 -2.3
Dopamine	10 µg/mL (65.3 µmol/L) 10 µg/mL (65.3 µmol/L)	1.02 mg/dL (90 µmol/L) 8.74 mg/dL (773 µmol/L)	-6.9 -2.1
Fluorocytosine	200 µg/mL (1549 µmol/L) 200 µg/mL (1549 µmol/L)	1.07 mg/dL (95 µmol/L) 7.94 mg/dL (702 µmol/L)	-0.9 -0.1
Levodopa (L-dopa)	15 µg/mL (76.1 µmol/L) 15 µg/mL (76.1 µmol/L)	1.03 mg/dL (91 µmol/L) 8.63 mg/dL (763 µmol/L)	-4.9 -2.3
Metamizole (Sulpyrine)	25 mg/dL (750 µmol/L) 25 mg/dL (750 µmol/L)	0.97 mg/dL (86 µmol/L) 8.37 mg/dL (740 µmol/L)	-5.2 -4.2
Methyl dopa	11.3 µg/mL (53.5 µmol/L) 11.3 µg/mL (53.5 µmol/L)	1.02 mg/dL (90 µmol/L) 7.47 mg/dL (660 µmol/L)	-8.8 -4.3
N-acetyl-p-benzoquinone imine (NAPQI)	0.4 mg/dL (26.8 µmol/L) 0.4 mg/dL (26.8 µmol/L)	1.02 mg/dL (90 µmol/L) 8.72 mg/dL (771 µmol/L)	-2.9 -0.3

Substance	Highest Concentration Tested with No Interference Conventional Units (SI Units)	Analyte Concentration Conventional Units (SI Units)	%
N-Acetyl Cysteine (NAC)	37.5 mg/dL (2.3 mmol/L) 37.5 mg/dL (2.3 mmol/L)	0.98 mg/dL (87 µmol/L) 8.36 mg/dL (739 µmol/L)	-7.1 -0.7
N-ethylglycine	0.4 mg/dL (38.3 µmol/L) 4.9 mg/dL (475.2 µmol/L)	0.99 mg/dL (88 µmol/L) 7.83 mg/dL (692 µmol/L)	6.1 9.5
Phenindione[a]	5 mg/dL (225 µmol/L) 5 mg/dL (225 µmol/L)	0.97 mg/dL (86 µmol/L) 7.76 mg/dL (686 µmol/L)	-5.2 -4.3
Phenylbutazone	321 µg/mL (1040.9 µmol/L) 321 µg/mL (1040.9 µmol/L)	0.99 mg/dL (88 µmol/L) 8.43 mg/dL (745 µmol/L)	-3.0 -1.5
Rifampicin	2.4 mg/dL (29.2 µmol/L) 2.4 mg/dL (29.2 µmol/L)	1.02 mg/dL (90 µmol/L) 8.57 mg/dL (758 µmol/L)	-2.0 -0.6
Salicylate	200 µg/mL (1448 µmol/L) 200 µg/mL (1448 µmol/L)	0.99 mg/dL (88 µmol/L) 8.41 mg/dL (743 µmol/L)	1.0 -0.2

[a] Refer to *Limitations*.

Urine

Substance	Highest Concentration Tested with No Interference Conventional Units (SI Units)	Analyte Concentration Conventional Units (SI Units)	%
6N HCl	0.01% 0.01%	41.72 mg/dL (3688 µmol/L) 188.42 mg/dL (16,656 µmol/L)	0.3 -0.6
pH 4	4.0 pH 4.0 pH	42.73 mg/dL (3777 µmol/L) 191.39 mg/dL (16,919 µmol/L)	-3.9 -2.3
pH 9	9.0 pH 9.0 pH	42.73 mg/dL (3777 µmol/L) 190.45 mg/dL (16,836 µmol/L)	-5.4 -3.8
Acetaminophen	200 mg/dL (13.2 mmol/L) 200 mg/dL (13.2 mmol/L)	40.36 mg/dL (3568 µmol/L) 183.14 mg/dL (16,190 µmol/L)	1.2 2.5
Acetic Acid	25 mL/24 hr collection 25 mL/24 hr collection	41.92 mg/dL (3706 µmol/L) 187.47 mg/dL (16,572 µmol/L)	-0.6 -0.6
Albumin	0.5 g/dL (5 g/L) 0.5 g/dL (5 g/L)	42.50 mg/dL (3757 µmol/L) 192.04 mg/dL (16,976 µmol/L)	-0.5 0.4
Ascorbate	3 mg/dL (199.9 µmol/L) 3 mg/dL (199.9 µmol/L)	41.94 mg/dL (3707 µmol/L) 190.30 mg/dL (16,823 µmol/L)	0.0 -0.4
Boric acid	1% w/v 1% w/v	42.69 mg/dL (3774 µmol/L) 190.59 mg/dL (16,848 µmol/L)	-0.4 -0.6
Conjugated bilirubin	50 mg/dL (855 µmol/L) 50 mg/dL (855 µmol/L)	37.01 mg/dL (3272 µmol/L) 168.09 mg/dL (14,859 µmol/L)	-0.9 -0.5
Ethanol	1 g/dL (216.9 mmol/L) 1 g/dL (216.9 mmol/L)	41.43 mg/dL (3662 µmol/L) 187.49 mg/dL (16,574 µmol/L)	0.2 -0.3
Gamma Globulin	0.5 g/dL (5 g/L) 0.5 g/dL (5 g/L)	42.71 mg/dL (3776 µmol/L) 192.42 mg/dL (17,010 µmol/L)	-0.5 -0.5

Substance	Highest Concentration Tested with No Interference Conventional Units (SI Units)	Analyte Concentration Conventional Units (SI Units)	%
Glucose	2000 mg/dL (111.1 mmol/L) 2000 mg/dL (111.1 mmol/L)	40.31 mg/dL (3563 µmol/L) 181.95 mg/dL (16,084 µmol/L)	0.6 0.7
Hemoglobin	100 mg/dL (1 g/L) 100 mg/dL (1 g/L)	40.34 mg/dL (3566 µmol/L) 178.21 mg/dL (15,754 µmol/L)	-0.3 0.6
Ibuprofen	500 mg/dL (24.3 mmol/L) 500 mg/dL (24.3 mmol/L)	40.34 mg/dL (3566 µmol/L) 183.38 mg/dL (16,211 µmol/L)	0.7 0.4
N-Acetylcysteine	2 mg/dL (122.6 µmol/L) 2 mg/dL (122.6 µmol/L)	40.06 mg/dL (3541 µmol/L) 180.00 mg/dL (15,912 µmol/L)	-0.1 0.1
Nitric Acid	0.6% 0.6%	42.49 mg/dL (3756 µmol/L) 187.60 mg/dL (16,584 µmol/L)	-0.2 0.3
Oxalic acid	0.1 g/dL (11.1 mmol/L) 0.1 g/dL (11.1 mmol/L)	40.31 mg/dL (3563 µmol/L) 182.59 mg/dL (16,141 µmol/L)	-0.3 -0.3
Sodium carbonate	5 g/24 hr collection 5 g/24 hr collection	40.15 mg/dL (3549 µmol/L) 180.93 mg/dL (15,994 µmol/L)	-0.6 -0.2

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

Standardization

The assay is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material SRM967.

Assigned values for calibrators are traceable to this standardization.

Technical Assistance

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

siemens-healthineers.com

References

1. Suzuki M, Yoshida M. A new enzymatic serum creatinine measurement based on an endogenous creatine-eliminating system. *Clinica Chimica Acta.* 1984;143(2):147-155.
2. 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.
3. Clinical and Laboratory Standards Institute. *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard—Seventh Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2017. CLSI Document GP41-A7.
4. 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.
5. 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.
6. Data on file at Siemens Healthcare Diagnostics.
7. Alberti MO, Drake TA, Song L. The pH of chemistry assays plays an important role in monoclonal immunoglobulin interferences. *Practical Laboratory Medicine*. 2015;3:8-16.

8. Sankaralingam A, Karim Y, Swaminathan R. Phenindione interferes with measurement of creatinine. *Clin Biochem*. 2013;46(18):1912–1913.
9. Roberts RT, Alexander NM, Kelner MJ. Definitive liquid-chromatographic demonstration that N-ethylglycine is the metabolite of lidocaine that interferes in the Kodak sarcosine oxidase-coupled method for creatinine. *Clin Chem*. 1988;34(12):2569-2572. PMID: 3197304.
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. Junge W, Wilke B, Halabi A, Klein G. Determination of reference intervals for serum creatinine, creatinine excretion and creatinine clearance with an enzymatic and a modified Jaffé method. *Clin Chim Acta*. 2004;344(1-2):137-48.
12. Wu AHB, ed. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. Philadelphia, PA: WB Saunders Company;2006:316.
13. 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.
14. 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.
15. 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.
16. 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; 2018. CLSI Document EP09c.
17. Clinical and Laboratory Standards Institute. *Interference Testing in Clinical Chemistry; Approved Guideline—Third Edition*. Wayne, PA: Clinical and Laboratory Standards Institute; 2018. CLSI Document EP07.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title	Symbol	Symbol Title
	Manufacturer	EC REP	Authorized representative in the European Community
	Use-by date	LOT	Batch code
REF	Catalog number		Contains sufficient for <n> tests
	Consult Instructions for Use	 Rev. XX	Version of Instructions for Use
 siemens.com/eifu	Internet URL address to access the electronic instructions for use	Rev. REVISION	Revision
IVD	*In vitro* diagnostic medical device	UDI	Unique Device Identifier
RxOnly	Prescription device (US only)	CE	CE Marking

Symbol	Symbol Title	Symbol	Symbol Title
CE XXXX	CE Marking with Notified Body		Keep away from sunlight
	Temperature limit		Lower limit of temperature
	Upper limit of temperature		Do not freeze
	Do not re-use		This way up
	Recycle		Caution
	Biological risks		Document face up[a]
UNITS C	Common Units	UNITS SI	International System of Units
YYYY-MM-DD	Date format (year-month-day)	YYYY-MM	Date format (year-month)
	Handheld barcode scanner		Mixing of substances
	Target		Interval
CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.	MATERIAL	Material
MATERIAL ID	Unique material identification number	CONTROL NAME	Name of control
CONTROL TYPE	Type of control	CAL LOT VAL	Calibrator lot value
CONTROL LOT VAL	Quality control lot value		

[a] Indicates Assay-*e*Note

Legal Information

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591 USA

Siemens Healthineers Headquarters
Siemens Healthcare GmbH
Henkestraße 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens-healthineers.com