SIEMENS Healthineers

C-Reactive Protein_2 (CRP_2)

Current Revision and Date[a]	Rev. 02, 2019-10	
Product Name	Atellica CH C-Reactive Protein_2 (CRP_2)	REF 11097631 (1000 tests)
Abbreviated Product Name	Atellica CH CRP_2	
Test Name/ID	CRP_2	
Systems	Atellica CH Analyzer	
Materials Required but Not Provided	Atellica CH CRP_2 CAL	REF 11099430
Specimen Types	Serum and plasma (lithium heparin)	
Sample Volume	4 µL	
Measuring Interval	0.4–30.4 mg/dL (4–304 mg/L)	

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

CE

Intended Use

The Atellica® CH C-Reactive Protein_2 (CRP_2) assay is for *in vitro* diagnostic use in the quantitative determination of the concentration of C-reactive protein in human serum and plasma (lithium heparin) using the Atellica® CH Analyzer. Such measurements are used in the evaluation of infection, tissue injury, inflammatory disorders, and associated diseases. Increases in C-reactive protein values are non-specific for many disease processes and should not be interpreted without a complete clinical evaluation.[1-4]

Summary and Explanation

The Atellica CH C-Reactive Protein_2 (CRP_2) assay measures CRP in serum and plasma by a latex-enhanced immunoturbidimetric assay. It is based on the principle that the analyte concentration is a function of the intensity of scattered light caused by the latex aggregates. The latex particles coated with anti-CRP antibodies rapidly agglutinate in the presence of C-reactive protein.

In most normal individuals, CRP is an acute-phase protein that is present in serum and plasma in very low concentrations. CRP serum concentrations become elevated in response to many pathological conditions, including infection, tissue injury, inflammatory disorders, and associated diseases. Increases in CRP values are non-specific for many disease processes and should not be interpreted without a complete clinical evaluation. Although elevated serum CRP levels are a non-specific response, serial measurement of CRP levels can be a valuable aid to diagnosis and management of the specific condition causing the elevation.

Principles of the Procedure

The Atellica CH C-Reactive Protein_2 (CRP_2) latex reagent is a suspension of uniform polystyrene latex particles coated with anti-CRP antibody. When serum or plasma containing CRP is mixed with the latex reagent, agglutination takes place resulting in an increase in the turbidity. This turbidity is measured at 571 nm. The CRP concentration in serum or plasma is determined from a calibration curve that is generated with the calibrators.

Reagents

Material Description	Storage	Stability[a]
Atellica CH CRP_2	Unopened at 2–8°C	Until expiration date on product
Pack 1 (P1)	Onboard per well	30 days
Well 1 (W1) Reagent 1 (R1) 15.1 mL Glycine (170 mmol/L); sodium chloride (100 mmol/L); EDTA disodium salt hydrate (50 mmol/L); sodium azide (0.09%)		
Well 2 (W2) Reagent 1 (R1) 15.1 mL Glycine (170 mmol/L); sodium chloride (100 mmol/L); EDTA disodium salt hydrate (50 mmol/L); sodium azide (0.09%)		
Pack 2 (P2)		
Well 1 (W1) Reagent 2 (R2) 15.1 mL CRP antibody synthetic latex (rabbit); sodium azide (0.09%)		
Well 2 (W2) Reagent 2 (R2) 15.1 mL CRP antibody synthetic latex (rabbit); 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.

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.

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 30 days per well. 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.[5]
- Follow recommended procedures for collection of diagnostic blood specimens by venipuncture.[6]
- Follow the instructions provided with your specimen collection device for use and processing.[7]
- Allow blood specimens to clot completely before centrifugation.[8]
- Keep tubes capped at all times.[8]

Storing the Specimen

Specimens may be stored for up to 3 days at 4–8°C or stored frozen for up to 6 months at -20°C or colder.[9]

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

This assay requires 4 µL of 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.

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

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

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[8]

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
11097631	**Pack 1 (P1)** Well 1 (W1) 15.1 mL of Atellica CH CRP_2 Reagent 1 Well 2 (W2) 15.1 mL of Atellica CH CRP_2 Reagent 1 **Pack 2 (P2)** Well 1 (W1) 15.1 mL of Atellica CH CRP_2 Reagent 2 Well 2 (W2) 15.1 mL of Atellica CH CRP_2 Reagent 2	2 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]	
11099430	Atellica CH CRP_2 CAL (calibrator)	1 x 1.0 mL calibrator level 1 CAL 1 1 x 1.0 mL calibrator level 2 CAL 2 1 x 1.0 mL calibrator level 3 CAL 3 1 x 1.0 mL calibrator level 4 CAL 4 1 x 1.0 mL calibrator level 5 CAL 5 1 x 1.0 mL calibrator level 6 CAL 6 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 40 µL of Reagent 1 into a reaction cuvette.
3. Dispenses 4 µL of pre-diluted sample into a reaction cuvette.

4. Dispenses 40 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: 8 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 CRP_2 assay, use Atellica CH CRP_2 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, if indicated by quality control results.

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	60
Pack Calibration	30
Reagent Onboard Stability	30

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 CRP_2 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 mg/dL (common units) or mg/L (SI units), depending on the units defined when setting up the assay.

Conversion formula: mg/dL x 10 = mg/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 Atellica CH CRP_2 assay is limited to the detection of concentration of C-reactive protein in human serum and plasma (lithium heparin).

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 potentially interfering substances.[10]

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

A reference interval for healthy adults was established in accordance with CLSI Document EP28-A3c and verified on the Atellica CH Analyzer.[11]

The reference interval for the concentration of C-reactive protein is < 1.0 mg/dL (< 10 mg/L) for adults.[12]

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.[11]

Performance Characteristics

Measuring Interval

The Atellica CH CRP_2 assay provides results from 0.4–30.4 mg/dL (4–304 mg/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 91.2 mg/dL (912 mg/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.[13] The assay is designed to have a limit of blank (LoB) ≤ limit of detection (LoD) and LoD ≤ 0.4 mg/dL (≤ 4 mg/L), and a limit of quantitation (LoQ) ≤ 0.4 mg/dL (≤ 4 mg/L) with ± 30% total allowable error.

The LoD corresponds to the lowest concentration of C-reactive protein that can be detected with a probability of 95%. The LoD for the Atellica CH CRP_2 assay is 0.0 mg/dL (0 mg/L), and was determined using 120 determinations, with 60 blank and 60 low level replicates, and a LoB of 0.0 mg/dL (0 mg/L).

The LoQ corresponds to the lowest amount of analyte in a sample that can be accurately quantitated with a total allowable error of 26.7%. The LoQ of the Atellica CH CRP_2 assay is 0.3 mg/dL (3 mg/L), and was determined using 180 determinations (multiple patient samples that were assayed using 3 reagent lots, over a period of 3 days, using total analytical error definition of bias + 2SD).

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

Precision

Precision was determined in accordance with CLSI Document EP05-A3.[14] 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		Designed to be ≤	Within-Lab Precision		Designed to be ≤
Sample Type	N	Mean mg/dL (mg/L)	SD[a] mg/dL (mg/L)	CV[b] (%)	CV (%)	SD mg/dL (mg/L)	CV (%)	CV (%)
Lithium heparin plasma	80	0.7 (7)	0.02 (0.2)	2.3	5	0.02 (0.2)	2.3	8
Serum	80	3.3 (33)	0.05 (0.5)	1.4	3	0.05 (0.5)	1.4	5
Serum	80	6.5 (65)	0.04 (0.4)	0.7	3	0.06 (0.6)	0.9	5
Serum	80	27.7 (277)	0.20 (2.0)	0.7	3	0.23 (2.3)	0.8	5

[a] Standard deviation.

[b] Coefficient of variation.

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

Assay Comparison

The Atellica CH CRP_2 assay is designed to have a correlation coefficient of > 0.950 and a slope of 1.00 ± 0.10 compared to ADVIA® Chemistry 1800 CRP_2. Assay comparison was determined using the Deming linear regression model in accordance with CLSI Document EP09-A3.[15] The following results were obtained:

Specimen	Comparative Assay (x)	Regression Equation	Sample Interval	N[a]	r[b]
Serum	ADVIA Chemistry 1800 CRP_2	y = 0.95x + 0.0 mg/dL (y = 0.95x + 0 mg/L)	0.6–30.3 mg/dL (6–303 mg/L)	100	0.989

[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.[15] The following results were obtained:

Specimen (y)	Reference Specimen (x)	Regression Equation	Sample Interval	N[a]	r[b]
Lithium heparin plasma	Serum	y = 1.02x - 0.1 mg/dL (y = 1.02x - 1 mg/L)	0.5–28.6 mg/dL (5–286 mg/L)	50	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)

The Atellica CH CRP_2 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 CRP_2 assay.[16]

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 Common Units (SI Units)	Analyte Concentration mg/dL (mg/L)	Percent Bias
Hemoglobin	750 mg/dL (0.465 mmol/L) 1000 mg/dL (0.621 mmol/L)	1.0 (10) 3.9 (39)	-4 -4
Bilirubin, conjugated	60 mg/dL (1026 µmol/L) 60 mg/dL (1026 µmol/L)	0.9 (9) 3.4 (34)	0 1
Bilirubin, unconjugated	60 mg/dL (1026 µmol/L) 60 mg/dL (1026 µmol/L)	1.0 (10) 3.7 (37)	0 2
Lipemia (Intralipid®)	1000 mg/dL (11.3 mmol/L) 1000 mg/dL (11.3 mmol/L)	1.0 (10) 3.9 (39)	0 -2

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 CRP_2 assay when present in serum at the concentrations indicated in the table below. Bias due to these substances is ≤ 10% at an analyte concentration of 0.5 mg/dL (5 mg/L).

Substance	Substance Test Concentration Common Units	Percent Bias
Rheumatoid factor	200 IU/mL	8

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

Prozone Effect

High CRP levels can cause a paradoxical decrease in signal as a result of the high-dose hook effect. In this assay, CRP levels as high as 100.0 mg/dL (1000 mg/L) will assay > 30.4 mg/dL (304 mg/L).

Standardization

The assay is traceable to the IRMM reference material ERMDA-470.

Assigned values for calibrators are traceable to this standardization.[17]

Technical Assistance

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

siemens.com/healthineers

References

1. Ng PC, Cheng SH, Chiu KM, *et al*. Diagnosis of the late onset neonatal sepsis with cytokines, adhesion molecule, and C-reactive protein in preterm very low birthweight infants. *Archives of Disease in Childhood--Fetal and Neonatal Edition*. 1997 Nov;77(3):221–227.
2. Claus DR, Osmand AP, Gewurz H. Radioimmunoassay of human C-reactive protein and levels in normal sera. *J Lab Clin Med.* 1976 Jan;87(1):120–128.
3. Konsensuswerte der DeutschenGesellschaft fur Laboratoriums-medizin, der DeutschenGesellschaft fur Klinische Chemie und des Verbandes der Diagnostica-Industrie e. V. (VDGH). *Clin Lab.* 1995; 41:743–748.
4. Kindmark CO. The concentration of C-reactive protein in sera from healthy individuals. *Scand J Clin Lab Invest.* 1972; Vol. 29, No. 4:407–111.
5. 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.
6. 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.
7. 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.

8. 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.
9. Tietz NW. *Clinical Guide to Laboratory Tests*. 4th ed. Philadelphia, PA. Saunders; 2006:190.
10. Young DS. *Effects of Drugs on Clinical Laboratory Tests*. 5th ed. Washington, DC: AACC Press; 2000.
11. 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.
12. Wu AHB, ed. *Tietz Clinical Guide to Laboratory Tests*. 4th ed. St. Louis, MO: Saunders; 2006:190–191.
13. 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.
14. 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.
15. 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.
16. 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.
17. Data on file at Siemens Healthcare Diagnostics.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Symbol Title and Description
	Consult instructions for use
 Rev. 01	Version of instructions for use
 siemens.com/healthcare  siemens.com/document-library	Internet URL address to access the electronic instructions for use
Rev. REVISION	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

Symbol	Symbol Title and Description
	Dangerous to environment
	Irritant Oral, dermal, or inhalation hazard
	Inhalation hazard Respiratory or internal health
	Flammable Flammable to extremely flammable
	Oxidizing
	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
IVD	*In vitro* diagnostic medical device
Σ (n)	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.

Symbol	Symbol Title and Description
	Mixing of substances Mix product before use.
	Reconstitute and mix lyophilized product before use.
	Target
	Interval
	Legal Manufacturer
EC REP	Authorized Representative in the European Community
	Use-by date Use by the designated date.
LOT	Batch code
REF	Catalog number
	Recycle
	Printed with soy ink
	CE Mark
	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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