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ADVIA® Chemistry XPT
Systems

Wide Range C-Reactive Protein (wrCRP)

Current Revision and Date[a]	Rev. H, 2020-02	
Product Name	ADVIA® Chemistry Wide Range C-Reactive Protein (wrCRP) Reagents	REF 03108390 (B01-4800-01) (2 × 220 tests per kit) REF 00829585 (7 × 315 tests per kit)
Systems	ADVIA Chemistry XPT System	
Materials Required but Not Provided	ADVIA Chemistry Wide-Range C-Reactive Protein Calibrators Reagent container adapters Commercially available controls	REF 00337402 (B03-4815-01)
Specimen Types	Human serum, plasma (lithium heparin)	
Assay Principle	Latex-enhanced immunoturbidimetric	
Assay Range[b]	Serum: 0.003–(15.6–16.4) mg/dL (0.03–[156–164] mg/L) Plasma: 0.003–(15.6–16.4) mg/dL (0.03–[156–164] mg/L)	
Reagent Storage	2–8°C	
Reagent On-System Stability	35 days	
Reagent Code	74038	

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

[b] The C-reactive protein concentration in the ADVIA Chemistry Wide-Range C-Reactive Protein Calibrator - Level 6 varies from 15.6–16.4 mg/dL (156–164 mg/L).

Intended Use

For *in vitro* diagnostic use in the quantitative measurement of the concentration of C-reactive protein in human serum and plasma on ADVIA® Chemistry XPT system. Such measurements are used in the detection and evaluation of infection, tissue injury, inflammatory disorders, and associated diseases. Increases in C-reactive protein (CRP) values are non-specific for many disease processes and should not be interpreted without a complete clinical evaluation.[1–4]

This method is referred to as wide-range C-reactive protein (wrCRP) because of the relatively wide analytical range that can be measured.

Summary and Explanation

The ADVIA Chemistry Wide Range C-Reactive Protein (wrCRP) assay measures CRP in serum and plasma by a latex-enhanced immunoturbidimetric method. 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 rapidly agglutinate in the presence of C-reactive protein-forming aggregates.

Principles of the Procedure

The ADVIA Chemistry wrCRP 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 calibrators.

Reagents

Reagent	Description	Storage	Reagent Stability
REF 03108390 (B01-4800-01)	**ADVIA Chemistry Wide Range C-Reactive Protein (wrCRP) Reagents**		
Wide Range C-Reactive Protein Reagent 1 wr CRP R1	13 mL in 20-mL containers Glycine (170 mmol/L) NaCl (100 mmol/L) Sodium EDTA disodium salt dihydrate (50 mmol/L) NaN_3 (0.09%, weight/volume)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 35 days
Wide Range C-Reactive Protein Reagent 2 wr CRP R2	13 mL in 20-mL containers anti-CRP antibody (rabbit) synthetic latex (lot specific) NaN_3 (0.09%, weight/volume)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 35 days
REF 00829585	**ADVIA Chemistry Wide Range C-Reactive Protein (wrCRP) Reagents**		
Wide Range C-Reactive Protein Reagent 1 wr CRP R1	18 mL in 20-mL containers Glycine (170 mmol/L) NaCl (100 mmol/L) Sodium EDTA disodium salt dihydrate (50 mmol/L) NaN_3 (0.09%, weight/volume)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 35 days
Wide Range C-Reactive Protein Reagent 2 wr CRP R2	18 mL in 20-mL containers anti-CRP antibody (rabbit) synthetic latex (lot specific) NaN_3 (0.09%, weight/volume)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 35 days

Warnings and Precautions

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

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 the 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.

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 and plasma (lithium heparin) for the ADVIA Chemistry wrCRP assay.

Follow these guidelines for specimens used for this assay:

- Serum and plasma can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[5] Follow the instructions provided with your specimen collection device for use and processing.[6]
- Complete clot formation should take place before 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.[7]
- 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 03108390 (B01-4800-01)	Reagent 1: 2 × 20-mL containers Reagent 2: 2 × 20-mL containers	2 × 220
REF 00829585	Reagent 1: 7 × 20-mL containers Reagent 2: 7 × 20-mL containers	7 × 315

Materials Required but Not Provided

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

Item	Description
REF 00337402 (B03-4815-01)	ADVIA Chemistry Wide-Range C-Reactive Protein Calibrators
REF 10316975	20-mL reagent container adapter for 40-mL slot
REF 10723030	20-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 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 wrCRP reagent is stable on the system for 35 days.

Do not use reagents beyond the expiration date.

Performing Calibration

To calibrate the ADVIA Chemistry wrCRP assay, use the ADVIA Chemistry Wide-Range C-Reactive Protein Calibrators, REF 00337402 (B03-4815-01).

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 21 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 ADVIA Chemistry Wide-Range C-Reactive Protein Calibrator - Level 1 as the sample for the RBL in this 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 C-reactive protein 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 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 C-reactive protein in mg/dL (common units) or mg/L (SI units).

Conversion factor: mg/dL × 10 = mg/L

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

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

The reference range for C-reactive protein is listed in the following table.[3–4]

Age	C-reactive Protein
Adults	0–0.5 mg/dL (0–5.0 mg/L)
Newborns, cord blood	< 0.06 mg/dL (< 0.6 mg/L)
Infants from 4th day of life to 1 month	< 0.16 mg/dL (< 1.6 mg/L)

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

The analytical range is from 0.003 mg/dL (0.03 mg/L) to the Wide-Range C-Reactive Protein Calibrator - Level 6, which varies from 15.6–16.4 mg/dL (156–164 mg/L).

Results that are below the low end of the assay range are flagged **< Conc Range**. You should report the test result as < 0.003 mg/dL (< 0.03 mg/L).

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

Extended Measuring Range

Siemens has validated an automatic rerun condition for this assay that extends the reportable range to 62.400 mg/dL (624.00 mg/L). You may configure the system to trigger automatic reruns. Rerun results will be flagged **Autorepeat**.

Prozone Effect

A prozone effect has been observed to occur at concentrations greater than 95 mg/dL (950 mg/L).

Testing was performed on an ADVIA Chemistry system with assay conditions identical to those on the ADVIA Chemistry XPT system.

Sensitivity

The ADVIA Chemistry wrCRP assay performance at low levels was analyzed as described in CLSI protocol EP17-A2, and the limit of blank (LoB) and limit of detection (LoD) were determined.[9]

The LoB is the highest measurement result that is likely to be observed on a blank sample. The LoB for the ADVIA Chemistry wrCRP assay is 0.001 mg/dL (0.01 mg/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 wrCRP assay is 0.003 mg/dL (0.03 mg/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 180 determinations with 120 blank and 60 low-level sample replicates.

Precision

The precision of the ADVIA Chemistry wrCRP assay was analyzed as described in CLSI protocol EP05-A2.[10] Each sample was assayed 3 times per run, 2 runs per day, for at least 10 days.

Precision: Common Units

			Repeatability (Within-Run)		Between-Run		Between-Day		Within-Lab (Total)	
Specimen Type	N	Mean (mg/dL)	SD[a] (mg/dL)	CV[b] (%)	SD (mg/dL)	CV (%)	SD (mg/dL)	CV (%)	SD (mg/dL)	CV (%)
Serum Control 1	60	0.727	0.004	0.5	0.006	0.9	0.009	1.2	0.012	1.6
Serum Control 2	60	2.855	0.010	0.4	0.021	0.7	0.028	1.0	0.036	1.3
Serum Control 3	60	5.247	0.065	1.2	0.019	0.4	0.068	1.3	0.096	1.8
Serum Pool 1	60	0.096	0.006	5.9	0.003	3.2	0.002	2.3	0.007	7.1
Serum Pool 2	60	0.514	0.003	0.6	0.006	1.2	0.004	0.8	0.008	1.6
Serum Pool 3	60	9.874	0.033	0.3	0.024	0.2	0.097	1.0	0.105	1.1

[a] SD = standard deviation

[b] CV = coefficient of variation

Precision: SI Units

			Repeatability (Within-Run)		Between-Run		Between-Day		Within-Lab (Total)	
Specimen Type	N	Mean (mg/L)	SD[a] (mg/L)	CV[b] (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)	SD (mg/L)	CV (%)
Serum Control 1	60	7.27	0.037	0.5	0.063	0.9	0.090	1.2	0.116	1.6
Serum Control 2	60	28.55	0.101	0.4	0.208	0.7	0.279	1.0	0.362	1.3

Specimen Type	N	Mean (mg/L)	Repeatability (Within-Run) SD[a] (mg/L)	Repeatability (Within-Run) CV[b] (%)	Between-Run SD (mg/L)	Between-Run CV (%)	Between-Day SD (mg/L)	Between-Day CV (%)	Within-Lab (Total) SD (mg/L)	Within-Lab (Total) CV (%)
Serum Control 3	60	52.47	0.645	1.2	0.191	0.4	0.684	1.3	0.959	1.8
Serum Pool 1	60	0.96	0.057	5.9	0.031	3.2	0.022	2.3	0.069	7.1
Serum Pool 2	60	5.14	0.030	0.6	0.062	1.2	0.043	0.8	0.081	1.6
Serum Pool 3	60	98.74	0.327	0.3	0.238	0.2	0.970	1.0	1.051	1.1

[a] SD = standard deviation

[b] CV = coefficient of variation

Actual results will vary depending on the study design, and on the sample and sample population used. Results obtained at individual laboratories may vary from the data provided.

Accuracy / Method Comparison

The performance of the ADVIA Chemistry wrCRP assay (y) was compared with the performance of the comparison assay on the indicated system (x).

Specimen Type	Comparison Assay (x)	N	r	Regression Equation	Sy.x	Sample Range
Serum	ADVIA 2400 wrCRP	66	1.000	y = 0.98x + 0.018 mg/dL y = 0.98x + 0.177 mg/L	0.114 mg/dL 1.138 mg/L	0.005–15.332 mg/dL 0.05–153.32 mg/L
Serum	ADVIA 1800 wrCRP	67	1.000	y = 0.99x + 0.017 mg/dL y = 0.99x + 0.174 mg/L	0.090 mg/dL 0.899 mg/L	0.005–15.556 mg/dL 0.05–155.56 mg/L
Plasma (Lithium Heparin)	ADVIA 1800 wrCRP	65	1.000	y = 1.02x + 0.003 mg/dL y = 1.02x + 0.035 mg/L	0.083 mg/dL 0.834 mg/L	0.700–13.543 mg/dL 7.00–135.43 mg/L
Plasma[a] (Lithium Heparin) ADVIA 1650/1800	ADVIA 1650 wrCRP - Serum	65	0.998	y = 0.99x - 0.004 mg/dL y = 0.99x - 0.04 mg/L	0.110 mg/dL 1.10 mg/L	0.02–6.98 mg/dL 0.20–69.8 mg/L

[a] Matrix comparison. Correlations between serum and plasma samples on ADVIA 1650 Chemistry systems are provided for reference.

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.

Interferences

Interferent	Interferent Level	C-Reactive Protein Sample Concentration	Interference
Bilirubin (conjugated)	50 mg/dL (855.0 µmol/L)	0.104 mg/dL (1.04 mg/L)	NSI[a]
	50 mg/dL (855.0 µmol/L)	0.292 mg/dL (2.92 mg/L)	NSI

Interferent	Interferent Level	C-Reactive Protein Sample Concentration	Interference
Bilirubin (unconjugated)	50 mg/dL (855.0 µmol/L)	0.103 mg/dL (1.03 mg/L)	NSI
	50 mg/dL (855.0 µmol/L)	0.291 mg/dL (2.91 mg/L)	NSI
Hemolysis (hemoglobin)	500 mg/dL (5.0 g/L)	0.091 mg/dL (0.91 mg/L)	NSI
	750 mg/dL (7.5 g/L)	0.091 mg/dL (0.91 mg/L)	-12.1%
	500 mg/dL (5.0 g/L)	0.277 mg/dL (2.77 mg/L)	NSI
	750 mg/dL (7.5 g/L)	0.277 mg/dL (2.77 mg/L)	-10.5%
Lipemia[b] (triglycerides from Intralipid)	1000 mg/dL (11.3 mmol/L)	0.089 mg/dL (0.89 mg/L)	NSI
	1000 mg/dL (11.3 mmol/L)	0.291 mg/dL (2.91 mg/L)	NSI

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

[b] SI units calculated as triolein

Note There is poor correlation between turbidity and triglyceride concentration in a lipemic sample.[11]

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 wrCRP assay is traceable to Institute for Reference Materials and Measurements (IRMM) certified reference material CRM 470. Recovery averaged 99% of the target concentration for the ADVIA 2400 Chemistry system (using the same reagent, with assay conditions identical to those on the ADVIA Chemistry XPT system). Assigned values of ADVIA Chemistry Wide-Range C-Reactive Protein Calibrators are traceable to this standardization.

Technical Assistance

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

siemens.com/healthcare

References

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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

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Intralipid is a trademark of Fresenius Kabi AB.

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