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ADVIA® Chemistry XPT
Systems

Rheumatoid Factor (RF)

Current Revision and Date[a]	Rev. G, 2019-07	
Product Name	ADVIA® Chemistry Rheumatoid Factor (RF) Reagents	REF 00655137 (B01-4806-01)
Systems	ADVIA Chemistry XPT System	
Materials Required but Not Provided	ADVIA Chemistry Liquid Specific Protein Calibrators Reagent container adapters Commercially available controls	REF 07711199 (B03-4845-01)
Specimen Types	Human serum	
Assay Principle	Latex-enhanced immunoturbidimetric	
Assay Range[b]	Serum: 8.4–(90.0–110.0) IU/mL	
Reagent Storage	2–8°C	
Reagent On-System Stability	60 days	
Reagent Code	74088	

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

[b] The RF concentration in the ADVIA Chemistry Liquid Specific Protein Calibrator - Level 6 varies from 90–110 IU/mL.

Intended Use

For *in vitro* diagnostic use in the quantitative measurement of rheumatoid factor in human serum on ADVIA® Chemistry XPT systems. Such measurements are used in the diagnosis of rheumatoid arthritis. Rheumatoid factors are auto-antibodies directed against the Fc portion of IgG. The majority of rheumatoid factors are IgM, but may be IgG or IgA. Conditions giving rise to such factors include rheumatic conditions and chronic inflammatory processes.[1–2]

Summary and Explanation

The ADVIA Chemistry Rheumatoid Factor (RF) assay measures rheumatoid factors in serum 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 the antibody rapidly agglutinate in the presence of the rheumatoid factors, forming aggregates.

Principles of the Procedure

The ADVIA Chemistry RF latex reagent is a suspension of uniform polystyrene latex particles coated with human IgG. When serum containing rheumatoid factor is mixed with the latex reagent, agglutination takes place resulting in an increase in the turbidity. This turbidity can be measured at 571 nm. The rheumatoid factor concentration in serum is determined from a calibration curve that is generated with a set of calibrators.

Reagents

Reagent	Description	Storage	Reagent Stability
REF 00655137 (B01-4806-01)	**ADVIA Chemistry Rheumatoid Factor (RF) Reagents**		
Rheumatoid Factor Reagent 1 RF R1	8.7 mL in 20-mL containers 3-[N-Morpholino] propane sulfonic acid buffer, pH 7.4 (25 mmol/L) NaN_3 (0.09%) Bovine serum albumin (1.0%)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 60 days
Rheumatoid Factor Reagent 2 RF R2	4.5 mL in 20-mL containers Human IgG synthetic latex (lot specific) NaN_3 (0.09%)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 60 days

Warnings and Precautions

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

Warning! Potential Biohazard

Contains human source material.

Caution: All products containing human source material should be treated as potentially infectious. Source material from human blood from which this product was derived was found negative when tested in accordance with current FDA required tests described in 21 CFR 610.40(a) and (b). No known test methods can offer assurance that products derived from human sources will not transmit infectious agents; this material should be handled using good laboratory practices and universal precautions.

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 for the ADVIA Chemistry RF assay.

Follow these guidelines for specimens used for this assay:

- Serum can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[3] Follow the instructions provided with your specimen collection device for use and processing.[4]
- Complete clot formation should take place before centrifugation.
- Serum should be physically separated from cells as soon as possible with a maximum limit of 2 hours from the time of collection.[5]
- Specimens should be free of particulate matter.
- Specimens should be as fresh as possible.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

Item	Contents	Number of Tests
REF 00655137 (B01-4806-01)	Reagent 1: 2 × 20-mL containers Reagent 2: 2 × 20-mL containers	2 × 100

Materials Required but Not Provided

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

Item	Description
REF 07711199 (B03-4845-01)	ADVIA Chemistry Liquid Specific 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 RF reagent is stable on the system for 60 days.

Do not use reagents beyond the expiration date.

Performing Calibration

To calibrate the ADVIA Chemistry RF assay, use the ADVIA Chemistry Liquid Specific Protein Calibrators, REF 07711199 (B03-4845-01).

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 60 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 Liquid Specific 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 rheumatoid factor 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 rheumatoid factor in IU/mL (common units or SI units).

Interpretation of Results

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

Limitations

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

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

Expected Values

Values < 14 IU/mL are within the normal serum range. This value is based on the determination of the serum samples from 100 normal individuals (97.5 percentile).[7]

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 8.4 IU/mL to the ADVIA Chemistry Liquid Specific Protein Calibrator - Level 6, which varies from 90.0–110.0 mg/L.

Results that are below the low end of the assay range are flagged **< Conc Range**. You should report the test result as < 8.4 IU/mL.

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 450.0 IU/mL. You may configure the system to trigger automatic reruns. Rerun results will be flagged **Autorepeat**.

Prozone Effect

Siemens found the prozone concentration for this method to be 450 IU/mL. The system software generates the flag, **Prozone (P)**, along with a result for sample to indicate a hook effect (prozone). These samples can be automatically diluted and rerun to obtain the correct RF concentrations.

All samples that are flagged for a prozone effect should be carefully reviewed by the laboratory and the physician in conjunction with the clinical status of the patient.

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

Sensitivity

The ADVIA Chemistry RF 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.[8]

The LoB is the highest measurement result that is likely to be observed on a blank sample. The LoB for the ADVIA Chemistry RF assay is 5.2 IU/mL.

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 RF assay is 8.4 IU/mL .

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 RF assay was analyzed as described in CLSI protocol EP05-A2.[9] Each sample was assayed 3 times per run, 2 runs per day, for at least 10 days.

Specimen Type	N	Mean (IU/mL)	Repeatability (Within-Run) SD[a] (IU/mL)	Repeatability (Within-Run) CV[b] (%)	Between-Run SD (IU/mL)	Between-Run CV (%)	Between-Day SD (IU/mL)	Between-Day CV (%)	Within-Lab (Total) SD (IU/mL)	Within-Lab (Total) CV (%)
Serum Control 1	60	27.7	0.49	1.8	0.29	1.0	0.00	0.0	0.57	2.0
Serum Control 2	60	52.5	0.39	0.7	0.24	0.4	0.00	0.0	0.46	0.9
Serum Control 3	60	62.1	0.89	1.4	0.43	0.7	0.00	0.0	0.99	1.6
Serum Pool 1	60	21.8	0.56	2.6	0.12	0.6	0.00	0.0	0.58	2.6
Serum Pool 2	60	69.2	0.48	0.7	0.24	0.4	0.29	0.4	0.61	0.9
Serum Pool 3	60	81.7	0.57	0.7	0.12	0.2	0.22	0.3	0.62	0.8

[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 RF 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 RF	82	0.999	y = 0.99x + 0.18 IU/mL	1.13 IU/mL	9.1–116.8 IU/mL
Serum	ADVIA 1800 RF	86	0.999	y = 1.04x + 0.19 IU/mL	1.17 IU/mL	8.4–110.6 IU/mL

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

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

Interferent	Interferent Level	Rheumatoid Factor Sample Concentration	Interference
Bilirubin (conjugated)	50 mg/dL (855 µmol/L)	24.7 IU/mL	NSI[a]
	50 mg/dL (855 µmol/L)	70.1 IU/mL	NSI
Bilirubin (unconjugated)	25 mg/dL (427.5 µmol/L)	25.3 IU/mL	NSI
	25 mg/dL (427.5 µmol/L)	71.9 IU/mL	NSI
Hemolysis (hemoglobin)	1000 mg/dL (10 g/L)	24.7 IU/mL	NSI
	1000 mg/dL (10 g/L)	69.1 IU/mL	NSI

Interferent	Interferent Level	Rheumatoid Factor Sample Concentration	Interference
Lipemia (triglycerides from Intralipid)	800 mg/dL (9.0 mmol/L)	25.0 IU/mL	NSI
	800 mg/dL (9.0 mmol/L)	70.8 IU/mL	NSI

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

Note There is poor correlation between turbidity and triglyceride concentration in a lipemic sample.[10]

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 RF assay is traceable to an internal standard manufactured using highly purified materials. Randox International Quality Assessment Scheme (RIQAS) survey samples were evaluated and found to recover on average 105% of the target concentrations on 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 Liquid Specific Protein Calibrators are traceable to this standardization.

Technical Assistance

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

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References

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3. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Guideline—Sixth Edition*. CLSI document GP41-A6. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.
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5. Clinical and Laboratory Standards Institute (formerly NCCLS). *Procedures for the Handling and Processing of Blood Specimens; Approved Guideline—Fourth Edition*. CLSI document GP44-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2010.
6. Young DS. *Effects of Drugs on Clinical Laboratory Tests*. 5th ed. Washington, DC: AACC Press; 2000.
7. Data on file at Siemens Healthcare Diagnostics.
8. Clinical and Laboratory Standards Institute (formerly NCCLS). *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline—Second Edition*. CLSI document EP17-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
9. Clinical and Laboratory Standards Institute (formerly NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition*. CLSI document EP05-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2004.
10. Twomey PJ, Don-Wauchope AC, McCullough D. Unreliability of triglyceride measurement to predict turbidity induced interference. *J Clin Pathol*. 2003 Nov;56(11):861–862.

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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