



OSR61105	RF Latex	
	4 x 24 mL	R1 RF Latex Buffer
	4 x 8 mL	R2 RF Latex

Intended Use

System reagent for the quantitative determination of Rheumatoid Factor (RF) in human serum and plasma on Beckman Coulter AU analyzers.

Summary^{1,2,3}

Rheumatoid factors (RF) are antibodies directed against antigenic determinants on the Fc fragment of IgG. These are usually IgM antibodies, but may be IgG, IgA or IgE.

Rheumatoid factor sensitivity in rheumatoid arthritis varies from 30% in population-based studies to 70 – 80% in hospital-based studies, where the disease tends to be more severe. Higher titres of RF are more specific for the diagnosis of rheumatoid arthritis (RA) and are more common in patients with rapidly progressive joint destruction and in those with extraarticular manifestations such as subcutaneous rheumatic nodules. However, RF is a non-specific test and a positive RF is observed in 1 – 5% of the healthy population at low titres and in 15 – 20% of elderly subjects with other chronic disease states. Similarly a negative result does not exclude RA. Approximately 25% of patients with a diagnosed case of RA may present with a negative result for RF.

A positive RF is also seen in autoimmune rheumatic diseases and in non-rheumatic conditions with variable frequency e.g. SLE, Sjögren's syndrome, subacute bacterial endocarditis and other bacterial infections, infectious hepatitis, chronic liver diseases, chronic active pulmonary diseases, parasitic infections and viral infections.

Methodology

Immune complexes formed in solution scatter light in proportion to their size, shape and concentration. Turbidimeters measure the reduction of incidence light due to reflection, absorption or scatter.

In this procedure, the decrease in light intensity transmitted (increase in absorbance) through particles suspended in solution is as a result of complexes formed during the immunological reaction between the RF of the patient serum and the anti-RF IgG antibodies coated on the latex particles.

System Information

AU400/400[®]/480, AU600,640/640[®]/680 and AU2700/5400/AU5800 Beckman Coulter Analyzers.

Reaction Principle

When a sample is mixed with R1 buffer and R2 IgG latex solution, RF reacts specifically with IgG coated on the latex particles to yield insoluble aggregates. The absorbance of these aggregates is proportional to the RF concentration in the sample.

Reagents

Final Concentration of Reactive Ingredients:

Glycine buffer (pH 8.0)	170 mmol/L
Latex coated with human IgG	< 0.5 %
Preservative	0.09 %

Precautions

OSHA Classification: Irritant

For *in vitro* diagnostic use.

Do not ingest. Harmful if swallowed.

Exercise the normal precautions required for handling all laboratory reagents.

Biological materials of human origin contained in R2 were tested for Anti-HCV, HbsAg and Anti-HIV 1/2 on a single donor basis using FDA approved methods and were found to be non-reactive. As there is no known test method that can offer complete assurance that products derived from human blood will not transmit infectious agents, this product should be handled as a potentially infectious material.

Contains sodium azide as a preservative, which may react with lead joints in copper plumbing to form explosive compounds. Even though the reagent contains minute quantities of sodium azide, drains should be well flushed with water when discarding the reagent.

Safety data sheet available for professional user on request.

Dispose of all waste material in accordance with local guidelines.

Preparation of Reagents

R1 is ready for use and can be placed directly on board the instrument. R2 should be mixed by inversion 5 – 10 times before placing on board the instrument and at weekly intervals thereafter.

Storage and Stability

The unopened reagent is stable until the expiration date printed on the label when stored at 2 - 8°C.

Working reagent is stable for 60 days when stored in the refrigerated compartment of the analyzer.

Indications of Deterioration

Visible signs of microbial growth, gross turbidity, precipitate or change in color in the RF Latex reagent may indicate degradation and warrant discontinuation of use.

RF Latex

Specimen Collection and Preparation

Serum, Li-heparin, and EDTA plasma.

Sample Storage and Stability⁴

Stable in serum and plasma for:

1 day at 20 – 25°C

8 days at 4 – 8°C

3 months at -20°C (avoid repeated freezing and thawing)

Interfering Substances

Results of studies show that the following substances may interfere with this RF procedure:

The criteria for no significant interference is recovery within 10% of the initial value

Bilirubin: No significant interference up to 40 mg/dL Bilirubin

Hemolysis: No significant interference up to 500 mg/dL Hemolysate

Lipemia: No significant interference up to 1000 mg/dL Intralipid*

* Intralipid, manufactured by KabiVitrium Inc., is a 20% IV fat emulsion used to emulate extremely turbid samples.

The information presented is based on results from Beckman Coulter studies and is current at the date of publication. Beckman Coulter Inc. makes no representation about the completeness or accuracy of results generated by future studies. For further information on interfering substances, refer to Young⁵ for a compilation of reported interferences with this test.

In very rare cases gammopathy, especially monoclonal IgM (Waldenström's macroglobulinemia), may cause unreliable results.

Procedure

A complete list of test parameters and operational procedure can be found in the User's Guide appropriate to the analyzer.

Materials Provided

System RF Latex Reagent

Materials required but not provided

RF Latex Calibrator (Cat. No. ODC0028)

0.9% Saline

Stability of Final Reaction Mixture

The Beckman Coulter chemistry analyzers automatically compute every determination at the same time interval.

Calibration

The frequency of calibration for the RF Latex procedure is every 30 days. Calibration of this procedure is accomplished by use of the RF Latex Calibrator ODC0028, which is traceable to WHO International reference material, NIBSC 64/2.⁶

For the zero calibrator use 0.9% saline.

Recalibration of this test is required when any of these conditions exist:

A reagent lot number has changed or there is an observed shift in control values.

Major preventative maintenance was performed on the analyzer.

A critical part was replaced.

Quality Control

During operation of the Beckman Coulter AU analyzer at least two levels of appropriate control material should be tested a minimum of once a day. In addition, these controls should be tested after calibration with each new lot of reagent and after specific maintenance or troubleshooting steps described in the appropriate User's Guide. Quality control testing should be performed in accordance with regulatory requirements and each laboratory's standard procedure.

Results

Automatically printed out for each sample in IU/mL at 37°C.

Dynamic Range

The RF Latex procedure is linear from 10 to 120 IU/mL. Samples exceeding the upper limit of linearity should be diluted with saline and repeated.

Prozone or hook effect may occur with high RF samples (300 – 2000 IU/mL). Prozone settings or data check parameters are required.

Expected Values⁷

Adult ≤ 14 IU/mL

This value is based on serum samples from 574 normal/healthy subjects (95th percentile).

Expected values may vary with age, sex, diet and geographical location. Each laboratory should determine its own expected values as dictated by good laboratory practice.

For diagnostic purposes, results should always be assessed in conjunction with the patient's medical history, clinical examinations and other findings.

Specific Performance Characteristics

The following data was obtained using the RF Latex reagent on Beckman Coulter AU analyzers according to established procedures. Results obtained in individual laboratories may differ.

Precision⁹

Estimates of precision, based on CLSI recommendations,⁸ are consistent with typical performance. The within run precision is less than 10% CV for RF values ≤ 20 IU/mL, less than 5% CV for RF values > 20 IU/mL and total precision is less than 10% CV. Assays of control material were carried out and data reduced following CLSI guidelines above.

N= 80	Within run		Total		
	Mean, IU/mL	SD	CV%	SD	CV%
	10.26	0.38	3.72	0.77	7.51
	20.06	0.45	2.24	0.79	3.96
	76.87	0.75	0.97	2.04	2.66
	114.81	0.93	0.81	2.97	2.59

Method Comparison⁹

Serum and plasma samples were used to compare this System RF Latex Reagent. The table below demonstrates representative performance on AU analyzers.

Y Method	AU640
X Method	Method 2
Slope	0.996
Intercept (IU/mL)	-1.217
Correlation Coeff. (r)	0.996
No. of Samples (n)	55
Range (IU/mL)	6.30 – 103.20

Sensitivity

The lowest detectable level was estimated as follows:

Analyzer	Lowest Detectable Level (IU/mL)
AU2700	1.38
AU640	1.42
AU400/680	2.22

Functional Sensitivity

Precision results (40-fold determination) for a level < 5.0 IU/mL have a CV of $< 20\%$ for each application.

	Mean Concentration (IU/mL)	SD	CV%
AU400	2.74	0.46	17.1
AU2700	3.09	0.53	17.2
AU640	3.22	0.54	16.9

Limit of Detection

The Limit of Detection (LOD) for RF was determined to be 4.74 IU/mL on the AU5800 analyzer. This was determined according to CLSI protocol EP17-A.¹⁰

Limit of Quantitation

The Limit of Quantitation (LOQ) for RF was determined to be 7.10 IU/mL on the AU5800 analyzer. This was determined according to CLSI protocol EP17-A¹⁰ and represents the lowest concentration of RF that can be measured with a total imprecision of 20%.

References

- Ismail AA, Snowden N. Autoantibodies and specific serum proteins in the diagnosis of rheumatological disorders. *Ann Clin Biochem* 1999;36:565-578.
- Mierau R, Genth E. Autoantibodies in rheumatoid arthritis. In: Thomas L, ed. *Clinical laboratory diagnostics. Use and assessment of clinical laboratory results.* Frankfurt/Main: TH-Books Verlagsgesellschaft, 1998:810-813.
- Shimmerling RH, Delbanco TL. The rheumatic factor: An analysis of Clinical Utility. *The American Journal of Medicine*, 1991; 91:530.
- Ehret W, Heil W, Schmitt Y, Töpfer G, Wisser H, Zawta B, et al. Use of Anticoagulants in Diagnostic Laboratory Investigations and Stability of Blood, Plasma and Serum Samples. WHO/DIL/LAB/99.1 Rev.2:41pp.
- Young DS. *Effects of drugs on clinical laboratory tests*, 6th ed. AACC Press, 2000.
- Anderson SG, Bentzon MW, Houba V, Krag P. International reference preparation of rheumatoid arthritis serum. *Bull Wld Hlth Org* 1970;42: 311-318.
- In-house data on file.
- CLSI/NCCLS. Evaluation of precision performance of clinical chemistry devices; approved guideline. CLSI/NCCLS document EP5-A;1999.
- Data is on file for specific AU analyzers.
- CLSI, protocol for determination of limit of detection and limit of quantitation; Approved guideline, EP17-A, 2004.

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