BECKMAN COULTER

AU/DxC AU US
Instructions For Use

RF (L)
RF Latex

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

For *in vitro* diagnostic use only.

For Rx use only

PRINCIPLE

INTENDED USE

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

SUMMARY AND EXPLANATION

Reference[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.

CHEMICAL REACTION SCHEME

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.

SPECIMEN

SPECIMEN STORAGE AND STABILITY

Reference[4]

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)

Specimen storage and stability information provides guidance to the laboratory. Based on specific needs, each laboratory may establish alternative storage and stability information according to good laboratory practice or from alternative reference documentation.

Additional handling conditions as designated by this laboratory:

SPECIMEN COLLECTION AND PREPARATION

Serum, Li-heparin, and EDTA plasma.

Additional instructions for patient sample preparation as designated by this laboratory:

Additional type conditions as designated by this laboratory:

REAGENTS

CONTENTS

System RF Latex Reagent

Reagent storage location in this laboratory:

WARNING AND PRECAUTIONS

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.
Dispose of all waste material in accordance with local guidelines.

This product contains material of animal origin. The product should be considered as potentially capable of transmitting infectious diseases.

REACTIVE INGREDIENTS

Final Concentration of Reactive Ingredients:

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

⚠ CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).
To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.

GHS HAZARD CLASSIFICATION

RF Latex R1

WARNING

H317	May cause an allergic skin reaction.
H402	Harmful to aquatic life.
P273	Avoid release to the environment.
P280	Wear protective gloves, protective clothing and eye/face protection.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before use.
	2-Methyl-4-isothiazolin-3-one < 0.06%

SDS	Safety Data Sheet is available at beckmancoulter.com/techdocs

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

RF Latex Calibrator (Cat. No. ODC0028)

0.9% Saline

Storage location of the Calibrator in this laboratory:

EQUIPMENT AND MATERIALS

For use on the AU480, AU680, AU5800, DxC 500 AU, DxC 500i and DxC 700 AU Beckman Coulter Analyzers.

Storage location of test tubes or sample cups in this laboratory:

REAGENT PREPARATION

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.

REAGENT 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.

Additional storage requirements as designated by this laboratory:

STABILITY OF FINAL REACTION MIXTURE

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

CALIBRATION

CALIBRATION INFORMATION

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 1st British Standard NIBSC code: 64/002[5]
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/DxC AU analyzer, at least two levels of an appropriate quality control material should be tested a minimum of once a day. In addition, controls should be performed after calibration with each new lot of reagent, and after specific maintenance or troubleshooting steps described in the appropriate Beckman Coulter AU/DxC AU analyzer Instructions For Use (IFU) and Reference Manual. Quality control testing should be performed in accordance with regulatory requirements and each laboratory's standard procedure.

Location of controls used at this laboratory.

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

A complete list of test parameters and operational procedures are provided in the relevant AU/DxC AU analyzer IFU and Reference Manual.

RESULTS INTERPRETATION

The default unit of measure is IU/mL.

REPORTING RESULTS

EXPECTED RESULTS

Reference[6]

Adult	≤ 14 IU/mL

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

Reference Intervals shown above were taken from the literature. Expected values may vary with age, sex, sample type, diet and geographical location. Each laboratory should verify the transferability of the expected values to its own population, and if necessary determine its own reference interval according to good laboratory practice. For diagnostic purposes, results should always be assessed in conjunction with the patient's medical history, clinical examinations and other findings.

Expected reference ranges in this laboratory:

INTERVALS	SAMPLE TYPE	UNITS (mg/dL)

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

INTERFERENCES

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 750 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. Further information on interfering substances is available.[7]

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

Laboratory specific procedure notes:

PERFORMANCE CHARACTERISTICS

PERFORMANCE CHARACTERISTICS

Data contained within this section is representative of performance on Beckman Coulter systems. Data obtained in your laboratory may differ from these values.

DYNAMIC RANGE / ANALYTICAL MEASURING RANGE

The RF Latex procedure is linear from 10 to 120 IU/mL Samples exceeding the upper limit of linearity should be manually diluted, using 1-part sample and 1-part physiological saline, repeated and the result multiplied by two. A concentration result is obtained from manually diluted samples in the >120 IU/mL - 240 IU/mL range. Dilution of samples above 240 IU/mL is not supported.

Prozone or hook effect may occur with high RF samples (300 – 2,000 IU/mL). Prozone settings or data check parameters are required.

SENSITIVITY

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.[8]

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-A[8] and represents the lowest concentration of RF that can be measured with a total imprecision of 20%.

METHODS COMPARISON

Reference[9]

Patient serum samples were evaluated in method comparison studies.

Results of Deming regression analysis were as follows:

Y Method	DxC 500 AU
X Method	DxC 700 AU
Slope	0.984
Intercept (IU/mL)	-0.083
Correlation Coeff. (r)	0.9995
No. of Samples (n)	104
Range (IU/mL)	11.05 - 114.28

PRECISION

Reference[9]

Estimates of precision, based on CLSI recommendations,[10] 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%**
17.17	0.47	2.7	0.58	3.4
51.73	0.26	0.5	0.41	0.8
102.55	0.49	0.5	0.70	0.7

ADDITIONAL INFORMATION

DxC 700 AU analyzers require that each reagent application has a standard format of abbreviated Test Name. This Test Name is required to allow automated loading of the calibrator information for each application. Refer to the table below for the Test Name assigned to each application for this assay.

Test Name	Description
RF-1G	RF LATEX (Serum)

Refer to the Beckman Coulter Chemistry Systems Reagent Guide (BAGUIDE) for specific chemistry information for the AU/DxC AU clinical chemistry systems and guidance on symbols used on all AU/DxC AU product labelling.

Setting Sheet Footnotes

User defined

Lot or Lot + Bottle

§ Saline should be used for the Zero calibrator

† RF Latex Calibrator Cat. No.: ODC0028

* Values set for working in IU/mL

REVISION HISTORY

Updated Calibration section

Preceding version revision history

Updated REPORTING RESULTS section

Updated PROCEDURAL NOTES section

Updated Performance Characteristics section

Updated References section

REFERENCES

1. Ismail AA, Snowden N. Autoantibodies and specific serum proteins in the diagnosis of rheumatological disorders. Ann Clin Biochem 1999;36:565-578.

2. 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.

3. Shimmerling RH, Delbanco TL. The rheumatic factor: An analysis of Clinical Utility. The American Journal of Medicine, 1991; 91:530.

4. 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.

5. Anderson SG, Bentzon MW, Houba V, Krag P. International reference preparation of rheumatoid arthritis serum. Bull Wld Hlth Org 1970;42: 311-318.

6. In-house data on file.

7. AACC Effects on Clinical Laboratory Tests: Drugs, Disease, Herbs and Natural Products https://clinfx.wiley.com/aaccweb/aacc/

8. CLSI, protocol for determination of limit of detection and limit of quantitation; Approved guideline, EP17-A, 2004.

9. Data is on file for specific AU/DxC AU analyzers.

10. CLSI. Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

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