RF (RHEUMATOID FACTOR)

En

REF 8A120	**5357**	**Tests**
REF 8A121	**3488**	**Tests**
REF BY120	**5973**	**Tests**
REF BY121	**3913**	**Tests**
REF At120	**1314**	**Tests**
REF DMT120	**1125**	**Tests**

Diagnostic reagent for determination of RF concentration.
Liquid. Dual reagents. Store at +2/+8°C. For in Vitro Diagnostic Use (IVD). Do not freeze
8A120/8A121/BY120/BY121/At120/DMT120 Products are Produced Specifically for Siemens Advia Siemens Atellica and Siemens Dimension Analyzer Series.
Changes made in the instructions for use are marked as grey.

INTENDED USE

The test is applied for the quantitative determination of RF in serum and plasma.

GENERAL INFORMATION

This antibody is directed against the Fc portion of the IgG molecule. Studies of monoclonal and polyclonal rheumatoid factor (RF) have demonstrated polireactive RF with binding specificity for substances other than IgG, such as nuclear components.[1] The polireactive RF is usually of IgM class with low affinity and develops against antigen within the joints of rheumatoid arthritis (RA) patients.[2] However, approximately 15% of RA patients have so-called seronegative RA and do not have serum autoantibodies. Patients with severe joint and systemic symptoms may also be found in this disease subgroup.[3]

IgM-RF is the main isotype identified by clinically available diagnostic assays for RF detection. RF tests are the most widely used serologic tests as an aid in the diagnosis of rheumatoid arthritis (RA)[4] more rarely IgA and IgG type RF have been detected.[5,6] IgA RF has been associated with more severe disease with erosions.[7] RF is not specific to RA and is frequently seen in chronic infections and other systemic inflammatory conditions as well.[1]

The etiology of RFs and their precise role in the pathogenesis of RA are still not fully understood although RF has proven to be a useful diagnostic and prognostic test. IgM-RF synthesis can be induced by immune complexes and polyclonal B cell activators. Transient synthesis of IgM-RF accompanies secondary immune responses and is part of the immunoregulatory process.

RF is produced during bacterial and viral infections, possibly in response to immune complexes containing microbial antigens. Polyclonal stimulation induces low affinity polyreactive IgM-RF, which can also be found in healthy individuals.[4]

TEST PRINCIPLE

Immunoturbidimetric method

Latex-bound, denatured IgG (antigen) reacts with RF antibodies in the sample to form antigen/antibody complexes and causes agglutination.

The absorbance of the agglutination-induced turbidity measured by turbidimetric method at a wavelength of 604 nm is proportional to the RF concentration in the sample.

REAGENT COMPONENTS

Reagent 1:

Tris buffer : ≤ 25 mmol/L
Sodium aside : ≤ 0.99 g/L
pH 8.2

Reagent 2:

Suspension of human gamma-globulin coated latex particles,
sodium aside : <0.99 g/L

REAGENT PREPARATION

Reagent is ready for use.

REAGENT STABILITY AND STORAGE

Reagents are stable at +2/+8°C till the expiration date stated on the label which is only for closed vials.

Once opened vials are stable for 30 days at +2/+8°C in optimum conditions. On board stability is strongly related to auto analyzers' cooling specification and carry-over values.

Reagent stability and storage data have been verified by using Clinical and Laboratory Standards Institute (CLSI) EP25-A protocol.[8]

SAMPLE REQUIREMENTS

Serum and plasma are collected by standard procedure. For plasma, sample collection tubes with Li heparin, K2 EDTA and K3 EDTA should be preferred.

RF activity stability in serum and plasma:

1 day at +20/+25ºC
8 days at +2/+8ºC
3 months at -20 ºC

CALIBRATION AND QUALITY CONTROL

Calibration: The assay requires the use of an RF Standard (Calibrator) Lyophilized. We recommend:

RF Standard (Calibrator) Lyophilized

Ref.No: TA121S

Calibration stability depends on the application characteristics and cooling capacity of the autoanalyzer used. Calibration stability is 30 days.

Control: Commercially available control material with established values determined by this method can be used. We recommend:

Specific Protein Control Level I (Rheumatoid Control I) Lyophilized

Ref.No: RCN01

Specific Protein Control Level II (Rheumatoid Control II) Lyophilized

Ref.No: RCN05

At least two level controls must be run once in every 24 hours. Each laboratory should determine its own quality control scheme and procedures. If quality control results are not within acceptable limits, calibration is required.

REFERENCE INTERVALS / MEDICAL DECISION LEVELS

Adult Serum[21] : 0 – 30 IU/mL

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary, determine its own reference range.

Reference interval has been verified by using CLSI EP28-A3c protocol.[9]

PERFORMANCE CHARACTERISTICS

Measuring Interval

According to CLSI EP34-ED1:2018, "Measuring Interval" refers to the interval where the analyte concentration is measured with intended accuracy in terms of medical and laboratory requirements without dilution, concentrating or any kind of pre-treatment that is between the analyte's lower limit of quantitation (LLoQ) and upper limit of quantitation (ULoQ).[10]

The determined analytic measuring interval for RF is 2 – 155 IU/mL.

Detection Capability

Limit of Detection (LoD): 1,5 IU/mL

Limit of Quantitation (LoQ): 2 IU/mL

Note: LoQ values are based on Coefficient of Variation Percentage (CV) ≤ 20%.

LoD and LoQ values have been verified by using CLSI EP17-A2:2012 protocol.[11]

Linearity

This method shows measurement linearity in the activities up to 155 IU/mL.

Autoanaylzer's auto-dilution system can be used if the concentrations have higher values. See device manual for further information.

For manual dilution procedure, dilute the sample 10-fold using 0.90% isotonic. After the dilution, multiply the result of rerun sample by the dilution factor. Do not report the sample result after dilution if it is marked as lower than the linear lower limit. Rerun with a suitable dilution.

Linearity Studies data have been verified by using CLSI EP06-A:2003 protocol.[12]

Precision

Running system has been developed according to 20x2x2 "The Single Site" protocol. Repeatability and Within-Laboratory Precision/Within-Device values have been obtained according to the running results.

According to the protocol in use, 2 separate runs per day have been made for 20 days (no obligation for being consecutive days). This protocol has been applied to each low and high samples separately and 80 results have been obtained for each one. Statistically, the results have been obtained using 2-factor Nested-ANOVA model.[13]

Repeatability (Within Run) and Repeatability (Day to Day) and CV% values of RF have been given in the table 1 and 2 respectively.

Table 1. RF Repeatability (Within Run) results obtained from samples in two different concentrations

Mean Concentration	SD	CV%	n
24,0 IU/mL	1,27	5.30	80
39,0 IU/mL	2,18	5,60	80

Note: This working system has been named "Within-Run Precision" in the previous CLSI - EP05-A2 manual.[14]

Table 2. RF Repeatability (Day to Day) results obtained from samples in two different concentrations

Mean Concentration	SD	CV%	n
24,0 IU/mL	1,58	6,60	80
39,0 IU/mL	2,38	6,10	80

Note: This working system has been named "Total Precision" in the previous CLSI - EP05-A2 manual.[14]

Method Comparison

As a result of the statistical evaluation of the method comparison data:

Passing-Babcock equation:[15]
y= 1.032x – 0.039 IU/mL
r=0.9999

Prozone Effect: No prozone effect has been observed up to 800 IU/mL tested for RF.

Interference

Endogenous interferant and analyte concentrations that have been used in the RF scanning tests has been determined according to "CLSI EP37-ED1:2018" and "CLSI EP07-ED3:2018" manuals.[16,17]

The total acceptable error rate, which is going to be used to detect whether the observed differential value obtained from RF interference scanning test is appropriate, is determined as ±25%.[18]

In RF test results, no significant interaction has been observed in the determined endogenous interferant and analyte concentrations or between interferants and analyte.

Hemoglobin : ≤ 10 g/L
Bilirubin : ≤ 20 mg/dL
Lipemia : ≤ 10 g/L

Annotation:

- All liquid-phase immunochemical assays may be sensitive to non-detection of antigen excess and should be treated cautiously.
- Drugs may affect RF concentration as follows:
  - ✓ Interferon α-2a and methotrexate may decrease serum RF levels;
  - ✓ Methyldopa, oral contraceptives and oxyphenicatin may increase serum RF levels;
  - ✓ Non-steroidal anti-inflammatory drugs may decrease serum RF levels or have nonsignificant effect on them.[19]

It should be noted that endogenous interferants, as well as various medicines and metabolites, anticoagulants (e.g. Heparin, EDTA, citrate, oxalate) and preservatives (e.g. sodium floride, iodoacetate, hydrochloride acide) such as additives, materials that may contact with samples during collection and processing (serum separator devices, sample collection containers and contents, catheters, catheter wash solutions, skin disinfectants, hand cleaners and lotions, glass washing detergents, powder gloves), dietary substances known to affect some specific tests (caffeine, beta-carotene, poppy seeds, etc.), or some substances present in a sample that cause foreign proteins (heterophilic antibodies, etc.), autoimmune response (autoantibodies, etc.), or due to malignancy (for example, interference by paraproteins with phosphate testing and indirect ion selective electrode methods) may show some negative effects that will cause various attempts and some misjudgements.[17]

These performance characteristics have been obtained using an autoanalyzer. Results may vary slightly when using different equipment or manual procedures.

WARNINGS AND PRECAUTIONS

IVD: For in Vitro Diagnostic use only.
Do not use expired reagents.
Reagents with two different lot numbers should not be interchanged.
For professional use.
Follow Good Laboratory Practice (GLP) guidelines.
Contains sodium azide.

CAUTION: Human source samples are processed with this product. All human source samples must be treated as potentially infectious materials and must be handled in accordance with OSHA (Occupational Safety and Health Administration) standards.

Danger

EUH032 :Releases a very toxic gas if contacts with acid.
H317 :May cause allergic skin reaction.

Precaution

P280 :Use protective gloves / clothes / glasses / mask.
P264 :Wash your hands properly after using.
P272 :Contaminated work clothes should not be allowed to be used outside of the workplace.

Intervention

P302+P352 :Wash with plenty of water and soap if it contacts with skin.
P333+P313 :Seek medical help if it irritates your skin or develops rash.
P362+P364 :Remove contaminated clothes and wash properly before using.

Disposal

P501 :Dispose the vials and contents according to the local regulations.

REFERENCES

1. McPherson, R. A., Pincus, M. R., (2017) Henry's Clinical Diagnosis and Management by Laboratory Methods (23rd ed.), Chapter 52: Clinical And Laboratory Evaluation of Systemic Rheumatic Diseases, p.993-1015.e7, Elsevier, St. Louis, Missouri 63043.
2. van Esch WJ, Reparon-Schuijt CC, Hamstra HJ, et al: Polyreactivity of human IgG Fc-binding phage antibodies

constructed from synovial fluid CD38+ B cells of patients with rheumatoid arthritis, J Autoimmun 19(4):241–250, 2002.
3. Ajeganova S, Huizinga TW: Rheumatoid arthritis: Seronegative and seropositive RA—Alike but different?, Nat Rev Rheumatol 11(1):8–9, 2015.
4. Kaplan, L., Pesce, A., (2010), Kaplan: Clinical Chemistry, 5th Edition: Clinical References – Methods of Analysis, Chapter: Rheumatoid Factor.
5. Bharadwaj A, Aggarawal A, Misra R: Clinical relevance of IgA rheumatoid factor (RF) in children with juvenile rheumatoid arthritis, Rheumatol Int 19(1/2):47–49, 1999.
6. Dorner T, Egerer K, Feist E, et al: Rheumatoid factor revisited, Curr Opin Rheumatol 16(3):246–253, 2004.
7. Houssien DA, Jonsson T, Davies E, et al: Clinical significance of IgA rheumatoid factor subclasses in rheumatoid arthritis, J Rheumatol 24(11):2119–2122, 1997.
8. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline. CLSI Document EP25-A. Wayne, PA: CLSI; 2009.
9. Clinical and Laboratory Standards Institute (CLSI). Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline – Third Edition. CLSI Document EP28-A3c. Wayne, PA: CLSI; 2010.
10. Clinical and Laboratory Standards Institute (CLSI). Establishing and Verifying an Extended Measuring Interval Through Specimen Dilution and Spiking – 1st Edition. CLSI Document EP34. Wayne, PA: CLSI; 2018.
11. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition. CLSI Document EP17-A2. Wayne, PA: CLSI; 2012.
12. Clinical and Laboratory Standards Institute (CLSI). Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach - 1st Edition. CLSI Document EP06-A. Wayne, PA: CLSI; 2003.
13. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition. CLSI Document EP05-A3. Wayne, PA: CLSI; 2014.
14. Clinical and Laboratory Standards Institute (CLSI). Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline - Second Edition. CLSI Document EP05-A2. Wayne, PA: CLSI; 2004.
15. Bablok W et al. A General Regression Procedure for Method Transformation. J Clin Chem Clin Biochem 1988;26:783-790.
16. Clinical and Laboratory Standards Institute (CLSI). Supplemental Tables for Interference Testing in Clinical Chemistry - First Edition. CLSI Document EP37. Wayne, PA: CLSI; 2018.
17. Clinical and Laboratory Standards Institute (CLSI). Interference Testing in Clinical Chemistry - Third Edition. CLSI Document EP07. Wayne, PA: CLSI; 2018.
18. CLIA proficiency testing criteria for acceptable analytical performance, as printed in the Federal Register July 11, 2022;87(131:41194-242.
19. Young DS. Effects of Drugs on Clinical Laboratory Tests. 4th ed. Washington, DC: AACC Press; 1995:3-527.
20. Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.
21. Tietz NW, editor. Clinical Guide to Laboratory Tests, 2nd ed. Philadelphia, PA: WB. Saunders, 1990.

SYMBOLS

IVD	In Vitro Diagnostic Medical Device
LOT	Lot Number
R1	Reagent 1
R2	Reagent 2
GTIN	Global Trade Item Number
REF	Reference Number
GLP	Good Laboratory Practices
FOR USE WITH	Identifies Products to Be Used Together
PRODUCT OF TURKEY	Product of Turkey
	Manufacturer
	Expiration Date
	Temperature Limits
	Consult Instructions for Use
	Caution
	Number of Tests

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