SIEMENS Healthineers

Dimension Vista®
System

RF Flex® reagent cartridge

Rheumatoid Factors

Revision bar indicates update to previous version.

Intended Use

The RF method is an *in vitro* diagnostic test for the quantitative measurement of rheumatoid factors (RF) in human serum and lithium heparinized plasma on the Dimension Vista® System. Measurements of RF are used as an aid in the diagnosis of rheumatoid arthritis.

Summary and Explanation

Rheumatoid factors are autoantibodies against the Fc region of human IgG which has been altered in its tertiary structure. These autoantibodies also react with animal IgG. Rheumatoid factors belong predominantly to the IgM class, but also occur in all other immunoglobulin classes[1,2].

The detection of RF is one of the criteria of the American Rheumatism Association (ARA) for the diagnosis of rheumatoid arthritis (RA)[3], since 70 - 90 % of patients with RA exhibit rheumatoid factors. Rheumatoid factors play an important role in the differential diagnosis between RA and other rheumatic diseases[1]. Moreover, they permit prognostic statements with regard to RA[4]. High RF concentrations are often associated with a more severe course of disease. There are, however, also seronegative types of RA without detectable RF. RF can occur in connection with other rheumatic and non-rheumatic diseases such as hepatitis, endocarditis, and parasitic or viral infections and other autoimmune diseases. With increasing age there is also an increase in the ratio of RF positive findings without corresponding signs of disease[1]. Therefore, the detection of RF alone cannot serve as diagnosis, but must be interpreted in conjunction with further clinical findings.

Rheumatoid factors were originally detected by the agglutination of sheep erythrocytes containing rabbit antibodies (Waaler-Rose Test), but then the agglutination of polystyrene particles coated with human IgG (Latex Test) won recognition[2]. The latter method can be easily automated and delivers standardized, quantitative results. The RF method combines elements of both detection procedures in that its polystyrene particles are coated with an immunocomplex of human and animal IgG.

Principles of the Procedure

Polystyrene particles coated with an immunocomplex consisting of human immunoglobulin and anti-human IgG from sheep are aggregated when mixed with samples containing RF. These aggregates scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

Reagents

Wells[a,b]	Form	Ingredient	Concentration[c]	Source
1–8	Liquid	RF Supplement Reagent:		
		Phosphate buffer;		
		Polyethylene glycol	~26 g/L	
9–12	Liquid	RF Reagent:		
		Polystyrene particles;	0.7 g/L	
		anti-human IgG;	2.7 mL/L	Sheep
		Human Immunoglobulin (16 %)	0.2 mL/L	

[a] Wells are numbered consecutively from the wide end of the cartridge.
[b] Contains Sodium azide (< 1 g/L) as a preservative.
[c] Nominal value per well in a cartridge.

Store at
2 to 8 °C.

Expiration
Refer to carton for expiration date of individual unopened reagent cartridges. Sealed wells on the instrument are stable for 90 days.

Open well stability
21 days for wells 1 - 12.

Warnings and Precautions

For *in-vitro* diagnostic use only.

For laboratory professional use.

Safety data sheets (MSDS/SDS) available on siemens-healthineers.com/sds.

CAUTION!
Federal (USA) law restricts this device to sale by or on the order of licensed healthcare professionals.

CAUTION! POTENTIAL BIOHAZARD
Each donor or donor unit was tested and found to be negative for human immunodeficiency virus (HIV) 1 and 2, hepatitis B virus (HBV) and hepatitis C virus (HCV) using either tests that are CE marked or FDA approved for this purpose. Because no known test can offer complete assurance of the absence of infectious agents, all human derived products should be handled with appropriate caution.

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.

Used cuvettes contain human body fluids; handle with appropriate care to avoid skin contact or ingestion.

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 all government requirements.

Reagent Preparation

All reagents are liquid and ready to use.

Specimen Collection and Handling

Collecting the Specimen

Recommended specimen types: serum or lithium heparinized plasma.

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].

For serum, 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 two hours from the time of collection[7].

Storing the Specimen

Samples should be as fresh as possible (stored for no more than seven days at 2 to 8 °C) or stored frozen. Samples can be stored at below –20 °C for up to three months, if they are frozen within 24 hours after collection and if repeated freeze-thaw cycles are avoided. Lipemic or frozen samples, which become turbid after thawing, must be clarified by centrifugation (10 minutes at approximately 15 000 x g) prior to testing. Specimens should be free of particulate matter.

Procedure

Materials Provided

REF	Contents	Number of Tests
K7068	Dimension Vista® RF Flex® reagent cartridge	2 × 200

Materials Required but not Provided

Item	Description
REF KC780	Dimension Vista® PROT2 CAL (Protein 2 Calibrator)
REF KS804	System Diluent
REF OUMT05	N DILUENT, N Diluent
REF KC785	Dimension Vista® PROT2 CON L (Protein 2 Control L (low))
REF KC787	Dimension Vista® PROT2 CON H (Protein 2 Control H (high))
Instruments, such as:	• Dimension Vista® 500 System • Dimension Vista® 1000T System • Dimension Vista® 1500 System • Dimension Vista® 3000T System

Test Steps

Sampling, reagent delivery, mixing, and processing are automatically performed by the Dimension Vista® System. For details of this processing, refer to your Dimension Vista® Operator's Guide.

	Test Conditions
Initial Sample Dilution	1:20
	Cuvette
Diluted Sample Volume (delivered to the cuvette)	13 µL
Diluent Volume	104.3 µL
Chase Volume	7 µL
RF Reagent	32.6 µL
Temperature	37 °C
Reaction time	6 minutes
Wavelength	840 nm
Type of Measurement	Nephelometric

Calibration

Calibration Material	PROT2 CAL, REF KC780
Calibration Scheme	7 levels, n = 3
Units	IU/mL
Typical Calibration Levels	0.43, 0.91, 1.94, 4.08, 8.61, 19.38, 38.75 IU/mL Multiply calibrator levels by the sample dilution to obtain the analytical measurement range. To obtain calibrator levels that span the measuring range, PROT2 CAL is diluted automatically with System Diluent by the instrument to the following dilutions: Level 1: 1:361 dilution Level 2: 1:171 dilution Level 3: 1:80 dilution Level 4: 1:38 dilution Level 5: 1:18 dilution Level 6: 1:8 dilution Level 7: 1:4 dilution
Calibration Frequency	Every 30 days for any one lot Calibration interval may be extended based on acceptable verification of calibration.
A new calibration is required:	• For each new lot of Flex® reagent cartridges • After major maintenance or service, if indicated by quality control results • As indicated in laboratory quality control procedures • When required by government regulations

Quality Control

Follow government regulations or accreditation requirements for quality control frequency. If not otherwise specified, analyze a minimum of two levels of a Quality Control (QC) material with known rheumatoid factors concentrations, e.g. PROT2 CON L or H at least once each day of use.

Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

Analytical Measurement Range (AMR)

10 – 600 IU/mL

This is the measuring range for the initial 1:20 dilution of samples that are automatically processed by the instrument. If the readings obtained are outside the initial measuring range, the method can be repeated using a higher dilution of the sample.

Refer to your Dimension Vista® Operator's Guide for information on repeat measurements using other dilutions.

- Samples with results in excess of 600 IU/mL can be repeated on a higher dilution.
- Samples with results less than 10 IU/mL will be reported as "less than 10 IU/mL" by the instrument.

Results

The instrument calculates the concentration of rheumatoid factors in IU/mL using the calculation scheme described in your Dimension Vista® Operator's Guide.

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

Limitations

Turbidity and particles in the samples may interfere with the determination. Therefore, samples containing particles must be centrifuged prior to testing. Lipemic or turbid samples, which cannot be clarified by centrifugation (10 minutes at approximately 15 000 x g), as well as heat inactivated samples, must not be used.

Due to matrix effects, inter-laboratory survey samples and control samples may yield results that differ from those obtained with other methods. It may therefore be necessary to assess these results in relation to method-specific target values.

The instrument reporting system contains flags and comments to provide the user with information regarding instrument processing errors, instrument status information and potential errors in rheumatoid factors results. Refer to your Dimension Vista® Operator's Guide for the meaning of report flags and comments. Any report containing flags and/or comments should be addressed according to your laboratory's procedure manual and not reported.

A negative result does not exclude rheumatoid arthritis. Approximately 25 % of patients with a diagnosed case of rheumatoid arthritis may present with a negative result for RF[8].

Certain non-rheumatoid conditions, connective tissue disorders and a variety of other disease states such as hepatitis may elicit a positive RF test.

The assay performance has not been established/tested for pediatric population.

Autoimmune antibodies common with other systemic autoimmune diseases were not assessed.

If a result exceeds the upper limit of the extended measuring range, it can be repeated by manual dilution.

Manual Dilution: Dilute with **N DILUENT** to obtain results within the analytical measurement range. Enter dilution factor on the instrument. Reassay. Results are multiplied by the dilution factor.

Expected Values

less than 15 IU/mL

Testing of serum from 300 European blood donors resulted in a 95th percentile of < 10 IU/mL and in a 97.5th percentile of 19.5 IU/mL.

Each laboratory should establish its own expected values for RF as performed on the Dimension Vista® System.

Performance Characteristics

The following data represent typical performance for the Dimension Vista® System.

Specificity

HIL Interference

The RF method was evaluated for interference according to CLSI EP7-A2[11]. Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10 % is considered interference.

Substance Tested	Substance Concentration[e]		RF IU/mL	Bias[d] (%)
Hemoglobin (hemolysate)	1 000 mg/dL	[0.155 mmol/L]	14.62	0
Bilirubin (unconjugated)	60 mg/dL	[1026 µmol/L]	12.05	-6
Bilirubin (conjugated)	60 mg/dL	[1026 µmol/L]	11.31	-7
Lipemia	Refer to "Specimen Collection and Handling", page 2 section			

[d] Analyte results should not be corrected based on this bias.

[e] Système International d'Unités [SI Units] are in brackets.

Maximum Observed Repeatability

The expected maximum observed standard deviations (SD) for repeatability (within-run precision) using n = 5 replicates at the following nominal RF concentrations are:

RF Concentration	Acceptable SD Maximum
80 IU/mL	6.2 IU/mL
210 IU/mL	14.8 IU/mL

A system malfunction may exist if the acceptable SD maximum is exceeded.

Precision[9,g]

Material	Mean (IU/mL)	Standard Deviation IU/mL (% CV)	
		Repeatability SD (IU/mL)	Within-Lab CV (%)
PROT2 CON L	73.7	1.5 (2.0)	1.6 (2.2)
PROT2 CON H	183.9	3.5 (1.9)	3.9 (2.1)
Serum pool[f]	14.5	0.9 (5.9)	0.9 (6.2)
Serum pool	30.5	0.8 (2.6)	1.8 (5.9)
Serum pool	90.0	2.1 (2.3)	2.3 (2.6)
Serum pool	544.3	21.7 (4.0)	23.9 (4.4)

[f] During each day of testing, two separate runs with one test sample were analyzed for 5 days.

[g] CLSI EP5-A2 was used. During each day of testing, two separate runs, with two test samples, for each test material, were analyzed for 20 days.

Method Comparison[10]

Regression Statistics[h]

Comparative Method	Slope	Intercept IU/mL	Correlation Coefficient	n
Roche TINA-QUANT RF II/Hitachi 917	0.953	– 9.71	0.95	120[i]

[h] CLSI EP9-A2 was used. The method used to fit the linear regression line was Passing Bablok.

[i] The range of RF values in the correlation study was 10 IU/mL to 520 IU/mL.

Non-Interfering Substances

The following substances do not interfere with the RF method when present in serum at the concentrations indicated. Inaccuracies (biases) due to these substances are less than 10 % at RF concentrations of 12.2 IU/mL to 316.9 IU/mL.

Substance	Test Concentration	SI Units
Acetaminophen	0.025 mg/dL	1.66 µmol/L
Amikacin	15 mg/dL	256 µmol/L
Ammonium heparin	3 U/mL	3 000 U/L
Ampicillin	5.3 mg/dL	152 µmol/L
Ascorbic acid	5 mg/dL	227 µmol/L
Caffeine	6 mg/dL	308 µmol/L
Carbamazepine	3 mg/dL	127 µmol/L
Chloramphenicol	5 mg/dL	155 µmol/L
Chlordiazepoxide	1 mg/dL	33.3 µmol/L
Chlorpromazine	0.2 mg/dL	6.27 µmol/L
Cholesterol	500 mg/dL	12.9 mmol/L
Cimetidine	2 mg/dL	79.2 µmol/L
Creatinine	30 mg/dL	2 652 µmol/L
Dextran 40	6 000 mg/dL	1 500 µmol/L
Diazepam	0.5 mg/dL	17.6 µmol/L
Digoxin	5 ng/mL	6.15 nmol/L
Erythromycin	6 mg/dL	81.6 µmol/L
Ethanol	400 mg/dL	86.8 mmol/L
Ethosuximide	25 mg/dL	1 770 µmol/L
Furosemide	6 mg/dL	181 µmol/L

Substance	Test Concentration	SI Units
Gentamicin	12 mg/dL	251 µmol/L
Ibuprofen	50 mg/dL	2 425 µmol/L
Immunoglobulin G (IgG)	5 g/dL	50 g/L
Lidocaine	1.2 mg/dL	51.2 µmol/L
Lithium chloride	2.3 mg/dL	3.2 mmol/L
Lithium heparin	3 U/mL	3 000 U/L
Nicotine	0.1 mg/dL	6.2 µmol/L
Penicillin G	25 U/mL	25 000 U/L
Pentobarbital	8 mg/dL	354 µmol/L
Phenobarbital	10 mg/dL	431 µmol/L
Phenytoin	5 mg/dL	198 µmol/L
Primidone	4 mg/dL	183 µmol/L
Propoxyphene	0.2 mg/dL	4.91 µmol/L
Protein, Albumin	6 g/dL	60 g/L
Salicylic acid	60 mg/dL	4.34 mmol/L
Sodium heparin	3 U/mL	3 000 U/L
Theophylline	4 mg/dL	222 µmol/L
Urea	500 mg/dL	83.3 mmol/L
Uric acid	20 mg/dL	1 190 µmol/L
Valproic acid	50 mg/dL	3 467 µmol/L

Hook Effect

The RF method shows no hook effect up to 2 877 IU/mL.

Recovery

Recovery of 1st British Standard 64/002[12] ranged from 96.4 - 98.6 % with a mean recovery of 97.9 %.

Limit of Detection

The limit of detection represents the lower limit of the reportable range for RF:
10 IU/mL

Technical Assistance

For customer support, contact your local technical support provider or distributor.
siemens-healthineers.com

Applicable Version of electronic Instructions for Use

As Siemens Healthineers continuously monitors the product performance and safety, the users are required to ensure that they work with the correct revision of the instructions for the product lots in use. Please periodically review the availability of new electronic labeling revisions to ensure safe use of the product.

The IFU version number is visible on each product box label. Siemens Healthineers ensures that all products lots bearing the same IFU version number are compatible with the electronic labeling provided via siemens-healthineers.com/eIFU.

References

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Definition of Symbols

The following symbols may appear on the product labeling:

	Do not reuse		Use By
LOT	Batch Code	REF	Catalogue Number
	Caution		Manufacturer
EC REP	Authorized representative in the European Community		Contains sufficient for <n> tests
	Biological Risks	IVD	*In Vitro* Diagnostic Medical Device
	Temperature Limitation		Consult instruction for Use
	Non-sterile	CE	CE marking of conformity
CE 0197	CE marking of conformity with notified body ID number. Notified body ID number can vary.	CONTENTS	Contents
	Reconstitution volume	LEVEL	Level
	Keep away from sunlight and heat	WARNING	Warning
DANGER	Danger	RxOnly	Prescription device (US only)
UDI	Device Identification (UDI) barcode	REACH xx/xx/xx	REACH Authorization Number

Legal Information

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