RF-II

cobas®

Rheumatoid Factors II

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
20764574 322	Rheumatoid Factors II 100 tests	System-ID 07 6457 4	**cobas c** 311, **cobas c** 501/502

Materials required (but not provided):

12172828 322	Preciset RF (5 x 1 mL)	Codes 725-729	
03005496 122	RF Control Set (4 x 1 mL)	Code 215 Level I	
		Code 216 Level II	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

For **cobas c** 311/501 analyzers:

RF-II: ACN 017

For **cobas c** 502 analyzer:

RF-II: ACN 8017

Intended use

In vitro test for the quantitative determination of Rheumatoid Factors (RF-II) in human serum and plasma on Roche/Hitachi **cobas c** systems. Measurements may be used as an aid in the diagnosis of rheumatoid arthritis.

Summary[1,2,3,4,5,6,7,8,9,10]

Rheumatoid factors are a heterogeneous group of autoantibodies directed against the antigenic determinants on the Fc-region of IgG molecules. They are important in the diagnosis of rheumatoid arthritis, but can also be found in other inflammatory rheumatic diseases and in various non-rheumatic diseases. They are also found in clinically healthy persons over 60 years of age. Despite these restrictions, the detection of rheumatoid factors is a diagnostic criterion of the American College of Rheumatology for classifying rheumatoid arthritis. The autoantibodies occur in all the immunoglobulin classes, although the usual analytical methods are limited to the detection of rheumatoid factors of the IgM type.

The classic procedure for the quantitation of rheumatoid factors is by agglutination with IgG-sensitized sheep erythrocytes or latex particles. Particular problems of these semiquantitative methods are the poor between-laboratory precision and reproducibility, together with standardization difficulties. For these reasons, new assay methods such as nephelometry, turbidimetry, enzyme-immunoassays and radioimmunoassays have been developed. The Roche RF assay is based on the immunological agglutination principle with enhancement of the reaction by latex.

Test principle[4,5,6]

Immunoturbidimetric assay.

Latex-bound heat-inactivated IgG (antigen) reacts with the RF-antibodies in the sample to form antigen/antibody complexes which, following agglutination, are measured turbidimetrically.

Reagents - working solutions

R1 Glycine buffer: 170 mmol/L, pH 8.0; polyethylene glycol: 0.05 %; bovine serum albumin; stabilizer; preservative

R2 Latex particles coated with human IgG; glycine buffer: 170 mmol/L, pH 7.3; stabilizer; preservative

R1 is in position B and R2 is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317 May cause an allergic skin reaction.

Prevention:

P261 Avoid breathing dust/fume/gas/mist/vapours/spray.

P272 Contaminated work clothing should not be allowed out of the workplace.

P280 Wear protective gloves.

Response:

P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.

P362 + P364 Take off contaminated clothing and wash it before reuse.

Disposal:

P501 Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590, USA: 1-800-428-2336

All human material should be considered potentially infectious. All products derived from human blood are prepared exclusively from the blood of donors tested individually and shown to be free from HBsAg and antibodies to HCV and HIV. The testing methods use assays that have been approved by the FDA or that are in compliance with the legal rules applicable to placing in vitro diagnostic medical devices for human use on the market in the European Union.
However, as no testing method can rule out the potential risk of infection with absolute certainty, the material should be handled with the same level of care as a patient specimen. In the event of exposure, the directives of the responsible health authorities should be followed.[11,12]

Reagent handling

Ready for use

Mix **cobas c** pack well before placing on the analyzer.

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

Storage and stability

RF-II

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	8 weeks

Diluent NaCl 9 %

RF-II

Rheumatoid Factors II

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	12 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum
Plasma: Li-heparin and K_2-EDTA plasma

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Stability:[13]	1 day at 20-25 °C
	8 days at 4-8 °C
	3 months at -20 °C (freeze only once)

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- See "Order information" section
- General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma

cobas c 311 **test definition**

Assay type	2-Point End		
Reaction time/Assay points	10 / 7-18		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Unit	IU/mL		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	–	
R2	30 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	6 µL	15 µL	135 µL
Increased	3 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End		
Reaction time/Assay points	10 / 12-26		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Unit	IU/mL		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	–	
R2	30 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	6 µL	15 µL	135 µL
Increased	3 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End		
Reaction time/Assay points	10 / 12-26		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Unit	IU/mL		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	–	
R2	30 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	6 µL	15 µL	135 µL
Increased	6 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2-6: Preciset RF
Calibration mode	RCM
Calibration frequency	Full calibration • after 180 days during shelf life • after reagent lot change • as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability:[14] This method has been standardized using the WHO Standard 64/2.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

cobas c systems automatically calculate the analyte concentration of each sample.

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at an RF concentration of 14 IU/mL.

Icterus:[15] No significant interference up to an I index of 40 for conjugated and 60 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 624 µmol/L or 40 mg/dL) and approximate unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[15] No significant interference up to an H index of 300 (approximate hemoglobin concentration: 186 µmol/L or 300 mg/dL).

Lipemia (Intralipid):[15] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[16,17]

High dose hook-effect: Using the prozone check, no false result without a flag was observed up to an RF concentration of 6000 IU/mL.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[18]

There is the possibility that other substances and/or factors may interfere with the test and cause unreliable results.

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

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

10-130 IU/mL

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

Lower limits of measurement

Lower detection limit of the test

10 IU/mL

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values

< 14 IU/mL

This value is based on serum samples from 541 test subjects.

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

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

Repeatability	*Mean*	*SD*	*CV*
	IU/mL	*IU/mL*	*%*
RF Control level 1	23.7	0.2	0.8
RF Control level 2	53.0	0.5	0.9
Human serum 1	19.5	0.3	1.6
Human serum 2	27.5	0.3	1.1

Intermediate precision	*Mean*	*SD*	*CV*
	IU/mL	*IU/mL*	*%*
RF Control level 1	23.2	0.3	1.4
RF Control level 2	51.4	0.8	1.5
Human serum 3	19.3	0.3	1.6
Human serum 4	26.1	0.5	1.8

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Method comparison

RF values for human serum and plasma samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Sample size (n) = 70

Passing/Bablok[19]	Linear regression
y = 1.000x - 1.20 IU/mL	y = 0.999x - 1.39 IU/mL
τ = 0.959	r = 0.998

The sample concentrations were between 10.8 and 114 IU/mL.

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

References

1 Borque L, Barozzi D, Ferrari L, et al. The Determination of Rheumatoid Factors by an Immunoturbidimetric Assay on Boehringer Mannheim/Hitachi Analysis Systems. Klin Lab 1994;40:445-453.

2 Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-324.

3 Bartfield H. Distribution of rheumatoid factor activity in non-rheumatoid states. Ann NY Acad Sci 1969;16:30-40.

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11 Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.

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13 Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.

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19 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

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