

Rheumatoid Factors II**Order information**

REF		CONTENT		Analyzer(s) on which cobas c pack(s) can be used
05480167190	05480167500	Rheumatoid Factors II (500 tests)	System-ID 03 6457 4	cobas c 701/702

Materials required (but not provided):

12172828322	Preciset RF (5 x 1 mL)	Codes 725-729	
	RF Control Set		
03005496122	Level I (2 x 1 mL)	Code 215	
	Level II (2 x 1 mL)	Code 216	
05172152190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3	

English**System information****RF-II:** ACN 8017**Intended use**

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

Summary

Measurements of rheumatoid factors with this assay in human serum and plasma may be used as an aid in the diagnosis of rheumatoid arthritis.

Rheumatoid factors are a heterogeneous group of autoantibodies directed against the antigenic determinants on the Fc-region of IgG molecules.¹ 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, however with low or moderate levels. Despite these restrictions, the detection of rheumatoid factors is a diagnostic criterion in several clinical guidelines for classifying rheumatoid arthritis.^{1,2,3,4,5}

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.^{6,7,8} This assay is based on the immunological agglutination principle with enhancement of the reaction by latex.

Test principle^{1,9,10}

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
- R3** Latex particles coated with human IgG; glycine buffer: 170 mmol/L, pH 7.3; stabilizer; preservative

R1 is in position B and R3 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.

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 mist or vapours.

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

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 or cleared by the FDA or that are in compliance with the legal rules of the European Union (IVDR 2017/746/EU, IVDD 98/79/EC, Annex II, List A). 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

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

Storage and stability

Shelf life at 2-8 °C: See expiration date on **cobas c** pack label.

On-board in use and refrigerated on the analyzer: 4 weeks

On-board on the Reagent Manager: 24 hours

Specimen collection and preparation

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

RF-II

Rheumatoid Factors II

Only the specimens listed below were tested and found acceptable.

Serum

Plasma: Li-heparin and K₂-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 (± 5 °C)

Freeze only once.

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 701/702 test definition

Assay type	2-Point End		
Reaction time / Assay points	10 / 21-29		
Wavelength (sub/main)	800/570 nm		
Reaction direction	Increase		
Unit	IU/mL		
Reagent pipetting		Diluent (H ₂ O)	
R1	90 µL	–	
R3	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 ₂ O S2-6: Preciset RF
Calibration mode	RCM
Calibration frequency	Full calibration - every 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 ± 1.4 IU/mL of initial values of samples ≤ 14 IU/mL and within ± 10 % for samples > 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. All special wash programming necessary for avoiding carry-over is available via the cobas link, manual input is required in certain cases. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SmpCln1+2/SCCS Method Sheet and for further instructions refer to the operator's manual.

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).

Values below the lower detection limit (< 10 IU/mL) will not be flagged by the instrument.

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.

PrecisionPrecision 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 on the **cobas c 701** analyzer:

Repeatability	Mean	SD	CV
	IU/mL	IU/mL	%
RF Control level 1	21.7	0.4	2.1
RF Control level 2	52.2	0.3	0.6
Human serum A	98.5	0.6	0.6
Human serum B	12.6	0.4	3.3
Human serum C	35.6	0.2	0.6
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

Results for intermediate precision were obtained on the **cobas c 501** analyzer.The data obtained on **cobas c 501** analyzer(s) are representative for **cobas c 701** analyzer(s).**Method comparison**RF values for human serum and plasma samples obtained on a **cobas c 701** analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c 501** analyzer (x).

Sample size (n) = 68

Passing/Bablok ¹⁹	Linear regression
$y = 1.024x - 0.911$ IU/mL	$y = 1.028x - 1.06$ IU/mL
$\tau = 0.965$	$r = 0.998$

The sample concentrations were between 10.8 and 113 IU/mL.

References

- Moore TL, Dorner RW. Rheumatoid factors. Clin Biochem 1993 Apr;26(2):75-84.
- Ingegnoli F, Castelli R, Gualtierotti R. Rheumatoid factors: clinical applications. Dis Markers 2013;35(6):727-734.
- Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010 Sep;69(9):1580-1588.
- Combe B, Landewe R, Daien CI, et al. 2016 update of the EULAR recommendations for the management of early arthritis. Ann Rheum Dis 2017 Jun;76(6):948-959.
- National Institute for Health and Care Excellence (NICE) (2018). Rheumatoid arthritis in adults: diagnosis and management. (NICE Guideline [NG100]) [updated 2020 October; cited 2024 February 15]. Available from: <https://www.nice.org.uk/guidance/ng100>.




- Bampton JL, Cawston TE, Kyle MV, et al. Measurement of rheumatoid factors by an enzyme-linked immunosorbent assay (ELISA) and comparison with other methods. Ann Rheum Dis 1985 Jan;44(1):13-19.
- Koopman WJ, Schrohenloher RE. A sensitive radioimmunoassay for quantitation of IgM rheumatoid factor. Arthritis Rheum 1980 Mar;23(3):302-308.
- Jaspers JP, Van Oers RJ, Leerkes B. Nine rheumatoid factor assays compared. J Clin Chem Clin Biochem 1988 Dec;26(12):863-871.
- Waalder E. On the occurrence of a factor in human serum activating the specific agglutination of sheep blood corpuscles. Acta Pathol Microbiol Scand 1940;17:172-178.
- Roberts-Thomson PJ, McEvoy R, et al. Ann Rheum Dis 1985;44:379-383.
- Occupational Safety and Health Standards: Bloodborne pathogens. (29 CFR Part 1910.1030). Fed. Register.
- Directive 2000/54/EC of the European Parliament and Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work.
- Use of Anticoagulants in Diagnostic Laboratory Investigations. WHO Publication WHO/DIL/LAB/99.1 Rev. 2: Jan 2002.
- Anderson SG, Bentzon MW, Houbav V, et al. International reference preparation of rheumatoid arthritis serum. Bull Wld Hlth Org 1970;42:311-318.
- Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.
- Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.
- Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.
- Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.
- 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:

	Contents of kit
	Volume for reconstitution
	Global Trade Item Number

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

COBAS, NAVIFY and PRECISET are trademarks of Roche.

All other product names and trademarks are the property of their respective owners.

Additions, deletions or changes are indicated by a change bar in the margin.

© 2024, Roche Diagnostics

05480167500V10.0

RF-II

Rheumatoid Factors II

CE 0123



Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com

+800 5505 6606



cobas®