RF-II

cobas®

Rheumatoid Factors II

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08058628190	08058628500	Rheumatoid Factors II (400 tests)	System-ID 2104 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

12172828322	Preciset RF (5 x 1 mL)	Codes 20725-20729	
03005496122	RF Control Set Level I (2 x 1 mL) Level II (2 x 1 mL)	 Code 20215 Code 20216	
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001	

English

System information

RF-II: ACN 21040

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:	8 weeks

RF-II

Rheumatoid Factors II

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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 (±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

Test definition

Reporting time	10 min	
Wavelength (sub/main)	800/570 nm	
Reagent pipetting		Diluent (H_2O)
R1	63 µL	–
R3	21 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.1 µL	–	–
Decreased	2.1 µL	20 µL	80 µL
Increased	2.1 µL	–	–

For further information about the assay test definitions refer to the application parameters screen of the corresponding analyzer and assay.

Calibration

Calibrators	S1: H_2O
	S2-6: Preciset RF
Calibration mode	Non-linear
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. It is recommended to perform quality control always after lot calibration and subsequently at least every 8 weeks. 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 in the unit IU/mL.

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 automatically performed by the analyzer, 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. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

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

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank	= 10 IU/mL
Limit of Detection	= 10 IU/mL
Limit of Quantitation	= 10 IU/mL

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration RF samples.

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. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Repeatability	*Mean* *IU/mL*	*SD* *IU/mL*	*CV* *%*
RF Control Level 1	21.8	0.509	2.3
RF Control Level 2	51.3	0.329	0.6
Human serum 1	15.0	0.704	4.7
Human serum 2	30.2	0.295	1.0
Human serum 3	37.9	0.250	0.7
Human serum 4	63.0	0.286	0.5
Human serum 5	109	0.707	0.6

Intermediate precision	*Mean* *IU/mL*	*SD* *IU/mL*	*CV* *%*
RF Control Level 1	21.8	0.550	2.5
RF Control Level 2	51.3	0.408	0.8
Human serum 1	15.0	0.704	4.7
Human serum 2	30.2	0.396	1.3
Human serum 3	39.5	0.365	0.9
Human serum 4	61.7	0.359	0.6
Human serum 5	109	0.773	0.7

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

RF values for human serum and plasma samples obtained on a **cobas c** 503 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 = 1.004x + 0.00648 IU/mL	y = 0.986x + 0.494 IU/mL
τ = 0.949	r = 0.996

The sample concentrations were between 12.6 and 121 IU/mL.

RF values for human serum and plasma samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Sample size (n) = 65

Passing/Bablok[19]	Linear regression
y = 1.037x - 1.61 IU/mL	y = 1.016x - 0.990 IU/mL
τ = 0.942	r = 0.995

The sample concentrations were between 11.8 and 125 IU/mL.

RF values for human serum and plasma samples obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Sample size (n) = 66

Passing/Bablok[19]	Linear regression
y = 1.026x - 1.70 IU/mL	y = 1.027x - 1.70 IU/mL
τ = 0.971	r = 0.999

The sample concentrations were between 11.4 and 130 IU/mL.

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.

References

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Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606