RF-II

Rheumatoid Factors II

cobas®

Specific proteins

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 INTEGRA 400 plus

Materials required (but not provided):

12172828 322	Preciset RF (5 x 1 mL)	System-ID 07 7995 4	
03005496 122	RF Control Set Level I (2 x 1 mL) Level II (2 x 1 mL)	 System-ID 07 8040 5 System-ID 07 9007 9	
20756350 322	NaCl Diluent 9 % (6 x 22 mL)	System-ID 07 5635 0	

English

System information

Test RF-II, test ID 0-757

Intended use

In vitro test for the quantitative immunological determination of human rheumatoid factors in serum and plasma on COBAS INTEGRA systems.

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 Reaction buffer
Glycine buffer: 170 mmol/L, pH 8.0; polyethylene glycol 0.05 %; bovine serum albumin; preservatives and stabilizers

SR Latex particles coated with human IgG; glycine buffer: 170 mmol/L, pH 7.3; preservatives and stabilizers

R1 is in position B and SR 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

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas c** pack label
On-board in use at 10-15 °C	8 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: Heparin (Li-, Na-) or EDTA (Na_2-, K_2-) 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

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)

1. NaCl Diluent 9 %, Cat. No. 20756350322, system-ID 07 5635 0 for automatic postdilution. NaCl Diluent 9 % is placed in its predefined rack position and is stable for 4 weeks on-board COBAS INTEGRA 400 plus analyzer.
2. NaCl 0.9 % (isotonic saline solution) for calibration.

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.

Application for serum and plasma

Test definition

Measuring mode	Absorbance
Abs. calculation mode	Endpoint
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A	583 nm
Calc. first/last	35/48
Typical prozone effect	> 600 IU/mL
Antigen excess check	Yes*
Unit	IU/mL

Pipetting parameters

		Diluent (H_2O)
R1	90 µL	
SR	30 µL	10 µL
Sample	3 µL	10 µL
Total volume	143 µL	

* Samples with concentrations > 130 IU/mL are flagged either >TEST RNG or "HIGH ACT". Rerun the sample with postdilution, or, if the sample has already been postdiluted, rerun the sample with a higher postdilution factor.

Calibration

Calibrator	Preciset RF
RF concentration	Lot-specific values. For calibration values, please refer to the assigned value sheet/barcode sheet obtained with Preciset RF.
Calibration mode	Logit/log 5
Calibration replicate	Duplicate recommended
Calibration interval	Each lot, every 180 days, and as required following quality control procedures.

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

Calibrators must be placed from the highest concentration first, to the lowest last, on the CAL/QC rack. 0 IU/mL calibrator is not provided with Preciset RF. Please use 0.9 % NaCl.

Traceability: This method has been standardized against the World Health Organization Reference Preparation for Rheumatoid Factors (1st preparation, 1970).[14]

Quality control

Quality control	RF Control Set
Control interval	24 hours recommended
Control sequence	User defined
Control after calibration	Recommended

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

The COBAS INTEGRA 400 plus analyzer automatically calculates the analyte concentration of each sample. For more details, please refer to Data Analysis in the Online Help.

Limitations - interference

Criterion: Recovery within ± 10 % of initial value.

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

Hemolysis:[15] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 0.621 µmol/L or 1000 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.

γ-Globulin: Due to the binding of RF to the Fc portion of IgG, pathologically high levels of γ-globulin (25 g/L) decrease the apparent RF concentration significantly.

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

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

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 INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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:
10.00 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 a zero sample (zero sample + 3 SD, repeatability, n = 30).

Expected values

In a study of 540 apparently healthy individuals, the expected reference range for RF was found to be less than 14 IU/mL.

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 COBAS INTEGRA 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 (1 aliquot per run, 1 run per day, 21 days). The following results were obtained:

	Level 1	Level 2
Mean	17 IU/mL	56 IU/mL
CV repeatability	2.3 %	1.3 %
CV intermediate precision	4.4 %	2.1 %

Method comparison

RF values for human serum samples obtained on a COBAS INTEGRA 400 analyzer with the COBAS INTEGRA Rheumatoid Factors II reagent (y) were compared with those determined using the same reagent for rheumatoid factors on a COBAS INTEGRA 700 analyzer (x) and a Roche/Hitachi 917 analyzer (x).

COBAS INTEGRA 700 analyzer

Sample size (n) = 50

Passing/Bablok[19]	Linear regression
y = 1.04x + 0.96	y = 1.02x + 1.69
τ = 0.953	r = 0.996
SD (md 95) = 3.601	Sy.x = 1.878

The sample concentrations were between 2.10 and 109.60 IU/mL.

Roche/Hitachi 917 analyzer	Sample size (n) = 50
Passing/Bablok[19]	Linear regression
y = 1.09x - 2.69	y = 1.08x - 2.45
τ = 0.958	r = 0.998
SD (md 95) = 3.009	Sy.x = 1.577

The sample concentrations were between 2.10 and 115.90 IU/mL.

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;168:30-40.

4 Waaler 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.

5 Moore TL, Dorner RN. Rheumatoid factors. Clin Biochem 1993;26:75-84.

6 Roberts-Thomson PJ, McEvoy R, Langhans T, et al. Ann Rheum Dis 1985;44:379-383.

7 Borque L, Yago M, Mar C, et al. Clin Chem 1986;32:124-129.

8 Bampton JL, Cawston TE, Kyle MV, et al. Ann Rheum Dis 1985;44:379-383.

9 Koopman WJ, Schrohenloker RE. Arthritis Rheum 1980;23:302-308.

10 Jaspers JP, Van Oers RJM, Leerkes B. Nine Rheumatoid Factor Assays Compared. J Clin Chem Clin Biochem 1988;26:863-871.

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

12 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.

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

14 Anderson SG, Bentzon MW, Houba V, et al. International reference preparation of rheumatoid arthritis serum. Bull Wld Hlth Org 1970;42:311-318.

15 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

16 Breuer J. Report on the Symposium "Drug Effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

17 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.

18 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

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

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

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.

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

RF-II

Rheumatoid Factors II

cobas®

Specific proteins

CE 0123

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