Rheumatoid Factors II

Order information

<table>
<thead>
<tr>
<th>REF</th>
<th>CONTENT</th>
<th>Analyzer(s) on which cobas c pack(s) can be used</th>
<th>System-ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>20764574 322</td>
<td>Rheumatoid Factors II 100 tests</td>
<td>System-ID 07 64574 4</td>
<td>Roche/Hitachi cobas c 311, cobas c 501/502</td>
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<tr>
<td>12172828 322</td>
<td>Preciset RF (5 x 1 mL)</td>
<td>Codes 725-729</td>
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</tr>
<tr>
<td>03005496 122</td>
<td>RF Control Set (4 x 1 mL)</td>
<td>Code 215 Level I</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Code 216 Level II</td>
<td></td>
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<tr>
<td>04489357 190</td>
<td>Diluent NaCl 9 % (50 mL)</td>
<td>System-ID 07 6869 3</td>
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</tr>
</tbody>
</table>

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
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 ast A antigen 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 semi-quantitative 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
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.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

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 applied were FDA-approved or cleared in compliance with the European Directive 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

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

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 %

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 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.

Stability:
1 day at 20-25 °C
8 days at 4-8 °C
3 months at -20 °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 311 test definition
### Assay Type: RF-II

<table>
<thead>
<tr>
<th>Component</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assay type</td>
<td>2-Point End</td>
</tr>
<tr>
<td>Reaction time/Assay points</td>
<td>10 / 7-18</td>
</tr>
<tr>
<td>Wavelength (sub/main)</td>
<td>800/570 nm</td>
</tr>
<tr>
<td>Reaction direction</td>
<td>Increase</td>
</tr>
<tr>
<td>Unit</td>
<td>IU/mL</td>
</tr>
<tr>
<td>Reagent pipetting</td>
<td>Diluent (H₂O)</td>
</tr>
<tr>
<td>R1</td>
<td>90 µL</td>
</tr>
<tr>
<td>R2</td>
<td>30 µL</td>
</tr>
<tr>
<td>Sample volumes</td>
<td>Sample dilution</td>
</tr>
<tr>
<td>Normal</td>
<td>3 µL</td>
</tr>
<tr>
<td>Decreased</td>
<td>6 µL, 15 µL, 135 µL</td>
</tr>
<tr>
<td>Increased</td>
<td>3 µL</td>
</tr>
</tbody>
</table>

#### 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 (H₂O)
- R1: 90 µL
- R2: 30 µL
- Sample volumes: Sample dilution
  - 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 (H₂O)
- R1: 90 µL
- R2: 30 µL
- Sample volumes: Sample dilution
  - Normal: 3 µL
  - Decreased: 6 µL, 15 µL, 135 µL
  - Increased: 6 µL

#### Calibration

- Calibrators: S1: H₂O, 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

- 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

- Roche/Hitachi cobas c systems automatically calculate the analyte concentration of each sample.

#### Limitations - Interference

- **Icterus:** No significant interference up to an L index of 40 for conjugated and 60 for unconjugated bilirubin. Approximate conjugated bilirubin concentration: 624 µmol/L or 40 mg/dL. Approximate unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL.
- **Lipemia (Intralipid):** No significant interference up to an L index of 300 (approximate hemoglobin concentration: 186 µmol/L or 300 mg/dL). 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. There is 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. There is the possibility that other substances and/or factors may interfere with the test and cause unreliable results.

#### Action Required

- **Special Wash Programming:** The use of special wash steps is mandatory when certain test combinations are run together on Roche/Hitachi cobas c systems. The latest version of the carry-over evasion list can be found with the NaOHDM-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 not required.
- 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<sup>19</sup>
<14 IU/mL
This value is based on serum samples from 525 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:

<table>
<thead>
<tr>
<th>Repeatability</th>
<th>Mean</th>
<th>SD</th>
<th>CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>IU/mL</td>
<td>IU/mL</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>RF Control level 1</td>
<td>23.7</td>
<td>0.2</td>
<td>0.8</td>
</tr>
<tr>
<td>RF Control level 2</td>
<td>53.0</td>
<td>0.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Human serum 1</td>
<td>19.5</td>
<td>0.3</td>
<td>1.6</td>
</tr>
<tr>
<td>Human serum 2</td>
<td>27.5</td>
<td>0.3</td>
<td>1.1</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Intermediate precision</th>
<th>Mean</th>
<th>SD</th>
<th>CV</th>
</tr>
</thead>
<tbody>
<tr>
<td>IU/mL</td>
<td>IU/mL</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>RF Control level 1</td>
<td>23.2</td>
<td>0.3</td>
<td>1.4</td>
</tr>
<tr>
<td>RF Control level 2</td>
<td>51.4</td>
<td>0.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Human serum 3</td>
<td>19.3</td>
<td>0.3</td>
<td>1.6</td>
</tr>
<tr>
<td>Human serum 4</td>
<td>26.1</td>
<td>0.5</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Method comparison
RF values for human serum and plasma samples obtained on a Roche/Hitachi cobas e 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<sup>20</sup>
Linear regression

\[
y = 1.0000x - 1.2091\text{ IU/mL} \\
y = 0.999x + 0.3912\text{ IU/mL} \\
\tau = 0.959 \\
r = 0.998
\]

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

References
19. Data on file at Roche Diagnostics.

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

**CONTENT**
- Contents of kit

**STIN**
- Volume after reconstitution or mixing

**GTIN**
- Global Trade Item Number

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