PRINCIPLE

INTENDED USE

RF reagent, when used in conjunction with SYNCHRON LX® System(s), UniCel® DxC 600/800 System(s) and SYNCHRON® Systems CAL 5 Plus, is intended for quantitative determination of rheumatoid factor concentration in human serum or plasma.

CLINICAL SIGNIFICANCE

Rheumatoid Factors are antibodies that react with the individual’s own immunoglobulin. The antibodies are usually directed against the Fc region of the IgG molecule. Rheumatoid Factor can be detected in the serum of the majority of patients with rheumatoid arthritis and is important for the diagnosis and prognosis of those patients with higher concentrations. These patients tend to suffer a more severe form of the illness and develop extra-joint complications more readily. Rheumatoid factors are not disease specific and can occur in lower frequencies in several other autoimmune disorders, chronic inflammation and normal individuals.

METHODOLOGY

RF reagent is used to measure rheumatoid factor concentration by a turbidimetric method. In the reaction, rheumatoid factor in the patient sample combines with specific antibody to form insoluble antigen-antibody complexes.

The SYNCHRON® System(s) automatically proportions the appropriate sample and reagent volumes into a cuvette. The ratio used is one part sample to 50 parts reagent. The system monitors the change in absorbance at 380 nanometers. This change in absorbance is proportional to the concentration of rheumatoid factor in the sample and is used by the System to calculate and express concentration of rheumatoid factor. A multi-point, nonlinear calibrator standard (in accordance with the World Health Organization) was used to establish lot-specific calibration parameters.

CHEMICAL REACTION SCHEME

\[
\text{RF} + \text{Latex - Human IgG} \rightarrow \text{Latex - Antigen - Antibody Complex (Antigen)}
\]
SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test. Freshly drawn serum or plasma are the preferred specimens. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood or urine are not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells within two hours from the time of collection.
2. Separated serum or plasma should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, serum or plasma may be stored at +2°C to +8°C for up to 7 days. Frozen samples are not recommended.

Additional specimen storage and stability conditions as designated by this laboratory:

SAMPLE VOLUME

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the Primary Tube Sample Template for your system.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.

Criteria for sample rejection as designated by this laboratory:

PATIENT PREPARATION

Special instructions for patient preparation as designated by this laboratory:
SPECIMEN HANDLING

Special instructions for specimen handling as designated by this laboratory:

REAGENTS

CONTENTS

Each kit contains the following items:

Two RF Reagent Cartridges (2 x 100 tests)
One lot-specific Parameter Card

VOLUMES PER TEST

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Volume</td>
<td>9 µL</td>
</tr>
<tr>
<td>ORDAC Sample Volume</td>
<td>4 µL</td>
</tr>
<tr>
<td>Total Reagent Volume</td>
<td>300 µL</td>
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</tbody>
</table>

Cartridge Volumes

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>A</td>
<td>250 µL</td>
</tr>
<tr>
<td>B</td>
<td>50 µL</td>
</tr>
<tr>
<td>C</td>
<td>– –</td>
</tr>
</tbody>
</table>

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Rheumatoid Factor Particle Reagent 36.3 mL
Rheumatoid Factor Reagent Buffer 7.4 mL

Also non-reactive chemicals necessary for optimal system performance.

⚠️ CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See National Institute for Occupational Safety and Health Bulletin: Explosive Azide Hazards (8/16/76).
CAUTION
Because this product is of human origin, it should be handled as though capable of transmitting infectious diseases. Each serum or plasma donor unit used in the preparation of this material was tested by United States Food and Drug Administration (FDA) approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HbsAg. Because no test method can offer complete assurance that HIV, hepatitis B virus, and hepatitis C virus or other infectious agents are absent, this material should be handled as though capable of transmitting infectious diseases. This product may also contain other human source material for which there is no approved test. The FDA recommends such samples to be handled as specified in Centers for Disease Control's Biosafety Level 2 guidelines.11

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT
SYNCHRON® Systems CAL 5 Plus
At least two levels of control material
Saline

REAGENT PREPARATION

NOTICE
Failure to mix the reagent prior to use will result in erroneous values.

1. Gently invert the cartridge several times prior to loading onto the system.
2. Check for bubbles or foam in compartments; break any bubbles.

ACCEPTABLE REAGENT PERFORMANCE
The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within your facility’s acceptance criteria.

REAGENT STORAGE AND STABILITY
RF reagent when stored unopened at +2°C to +8°C, will obtain the shelf-life indicated on the cartridge label. Once opened, the reagent is stable for 60 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

Reagent storage location:

CALIBRATION
CALIBRATOR REQUIRED
SYNCHRON® Systems CAL 5 Plus

CALIBRATOR PREPARATION
No preparation is required.
CALIBRATOR STORAGE AND STABILITY

SYNCHRON® Systems CAL 5 Plus is stable until the expiration date printed on the calibrator bottle if stored capped in the original container at +2°C to +8°C.

⚠️ CAUTION

Because this product is of human origin, it should be handled as though capable of transmitting infectious diseases. Each serum or plasma donor unit used in the preparation of this material was tested by United States Food and Drug Administration (FDA) approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HbsAg. Because no test method can offer complete assurance that HIV, hepatitis B virus, and hepatitis C virus or other infectious agents are absent, this material should be handled as though capable of transmitting infectious diseases. This product may also contain other human source material for which there is no approved test. The FDA recommends such samples to be handled as specified in Centers for Disease Control’s Biosafety Level 2 guidelines.11

Calibrator storage location:

CALIBRATION INFORMATION

1. The system must have a lot-specific parameter card and a valid calibration adjustment in memory before controls or patient samples can be run.

2. Under typical operating conditions the RF reagent cartridge must be calibrated every 30 days and also with certain parts replacements or maintenance procedures, as defined in the SYNCHRON LX Maintenance Manual and Instrument Log, or the UniCel DxC 600/800 System Instructions For Use (IFU) manual. This assay has within-lot calibration available. Refer to the SYNCHRON LX Operations Manual, or the UniCel DxC 600/800 System Instructions For Use (IFU) manual for information on this feature.

3. For detailed calibration instructions, refer to the SYNCHRON LX Operations Manual, or the UniCel DxC 600/800 System Instructions For Use (IFU) manual.

4. The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the SYNCHRON LX Diagnostics and Troubleshooting Manual, or the UniCel DxC 600/800 System Instructions For Use (IFU) manual.

TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

QUALITY CONTROL

At least two levels of control material should be analyzed daily. In addition, these controls should be run with each new calibration, with each new reagent cartridge, and after specific maintenance or troubleshooting procedures as detailed in the appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.
The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

Table 1.0 Quality Control Material

<table>
<thead>
<tr>
<th>CONTR OL NAME</th>
<th>SAMPLE TYPE</th>
<th>STORAGE</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>

TESTING PROCEDURE(S)

1. If necessary, load the reagent onto the system. A lot-specific parameter card must be loaded one time for each lot.
2. After reagent load is completed, calibration may be required.
3. Program samples and controls for analysis.
4. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the SYNCHRON LX Operations Manual, or the UniCel DxC 600/800 System Instructions For Use (IFU) manual.

CALCULATIONS

The SYNCHRON® System(s) performs all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

REPORTING RESULTS

Equivalency between the SYNCHRON LX and UniCel DxC 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

REFERENCE INTERVALS

Greater than 95% of a group of 125 apparently healthy adults in Southern California showed no detectable RF (<20 IU/mL) with this assay. Published “upper limits of normal” vary widely among different sources. Each laboratory must establish its own reference interval based on its patient population. The presence of RF in patient serum should be considered as one criterion of rheumatoid disease, and not as a definitive diagnosis.

Table 2.0 Reference intervals

<table>
<thead>
<tr>
<th>INTERVALS</th>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYNCHRON</td>
<td>Serum or Plasma</td>
<td>&lt; 20 IU/mL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INTERVALS</th>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

1. If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method based on a study of 20 healthy volunteers:

<table>
<thead>
<tr>
<th>ANTICOAGULANT</th>
<th>LEVEL TESTED FOR IN VITRO INTERFERENCE</th>
<th>AVERAGE PLASMA-SERUM BIAS (IU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lithium Heparin</td>
<td>14 Units/mL</td>
<td>NSI$^b$</td>
</tr>
<tr>
<td>Sodium Heparin</td>
<td>14 Units/mL</td>
<td>NSI</td>
</tr>
</tbody>
</table>

   a Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.
   b NSI = No Significant Interference (within ±20 IU/mL or 8%).

2. The following anticoagulants were found to be incompatible based on the same study:

<table>
<thead>
<tr>
<th>ANTICOAGULANT</th>
<th>LEVEL TESTED FOR IN VITRO INTERFERENCE</th>
<th>PLASMA-SERUM BIAS (IU/mL)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDTA</td>
<td>1.5 mg/dL</td>
<td>+180</td>
</tr>
</tbody>
</table>

   a Bias is based on worst case instead of average. Plus (+) or minus (-) signs in this column signify positive or negative bias.

LIMITATIONS

None identified.

INTERFERENCES

1. The following substances were tested for interference with this methodology:

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>SOURCE</th>
<th>LEVEL</th>
<th>OBSERVED EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>RBC hemolysate</td>
<td>500 mg/dL</td>
<td>NSI$^b$</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Bovine</td>
<td>30 mg/dL</td>
<td>NSI</td>
</tr>
<tr>
<td>Lipemia</td>
<td>Intralipid$^c$</td>
<td>400 mg/dL</td>
<td>NSI</td>
</tr>
</tbody>
</table>

   a Data shown was collected using SYNCHRON CX Systems. Equivalency between SYNCHRON LX Systems has been established by Deming regression analysis to SYNCHRON CX Systems.
   b NSI = No Significant Interference (within ±20 IU/mL or 8%).
   c Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250.
2. Serum samples may yield different concentration values for rheumatoid factor when analyzed at various dilutions. This phenomenon may be caused by the presence of rheumatoid factor complexes with inhibitors or interfering substances present in the serum. Sample dilution will reduce the effective concentration of the interfering substances so that the final result obtained for rheumatoid factor in the diluted sample will be increased over the result obtained for the undiluted (neat) or lesser diluted sample.

3. Refer to References (15,16,17) for other interferences caused by drugs, disease and preanalytical variables.

**PERFORMANCE CHARACTERISTICS**

**ANALYTIC RANGE**

The SYNCHRON® System(s) method for the determination of this analyte provides the following analytical range:

<table>
<thead>
<tr>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum or Plasma</td>
<td>20 – 800 IU/mL</td>
</tr>
<tr>
<td>Serum or Plasma (ORDAC)</td>
<td>650 – 1770 IU/mL</td>
</tr>
</tbody>
</table>

Samples with concentrations outside of the analytical range will be reported as ";<20 IU/mL" or ";>800 IU/mL" (ORDAC ";<650 IU/mL" or ";>1770 IU/mL").

Samples reported out as greater than the analytical range should be confirmed by enabling ORDAC, or diluting with saline, and reanalyzing. If manual dilution is used the appropriate dilution factor should be applied to the reported result.

Samples reported out as "SUPPRESSED" due to RXN ERROR should be reanalyzed.

**REPORTABLE RANGE (AS DETERMINED ON SITE):**

<table>
<thead>
<tr>
<th>SAMPLE TYPE</th>
<th>CONVENTIONAL UNITS</th>
<th>S.I. UNITS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**SENSITIVITY**

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for RF determination is 20 IU/mL.

**EQUIVALENCY**

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

**Serum or Plasma (in the range of 21 to 590 IU/mL):**

\[
Y \text{ (SYNCHRON LX Systems)} = 1.104X - 7.56 \\
N = 86 \\
\text{MEAN (SYNCHRON LX Systems)} = 142.9 \\
\text{MEAN (IMMAGE® RF)} = 136.3 \\
\text{CORRELATION COEFFICIENT (r)} = 0.973
\]
Refer to References (18) for guidelines on performing equivalency testing.

**PRECISION**

A properly operating SYNCHRON® System(s) should exhibit precision values less than or equal to the following:

**Table 8.0 Precision Values**

<table>
<thead>
<tr>
<th>TYPE OF PRECISION</th>
<th>SAMPLE TYPE</th>
<th>1 SD</th>
<th>CHANGEOVER VALUE&lt;sup&gt;a&lt;/sup&gt;</th>
<th>% CV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serum/Plasma</td>
<td>10.0</td>
<td>250</td>
<td>4.0</td>
</tr>
<tr>
<td>Within-run</td>
<td>Serum/Plasma (ORDAC)</td>
<td>NA&lt;sup&gt;b&lt;/sup&gt;</td>
<td>NA</td>
<td>10.0</td>
</tr>
<tr>
<td>Total</td>
<td>Serum/Plasma</td>
<td>15.0</td>
<td>250</td>
<td>6.0</td>
</tr>
<tr>
<td></td>
<td>Serum/Plasma (ORDAC)</td>
<td>NA</td>
<td>NA</td>
<td>15.0</td>
</tr>
</tbody>
</table>

<sup>a</sup> When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

<sup>b</sup> NA = Not applicable.

Comparative performance data for a SYNCHRON LX® System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below. Each laboratory should characterize their own instrument performance for comparison purposes.

**Table 9.0 NCCLS EP5-T2 Precision Estimate Method**

<table>
<thead>
<tr>
<th>TYPE OF IMPRECISION</th>
<th>SAMPLE TYPE</th>
<th>No. Systems</th>
<th>No. Data Points&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Test Mean Value (IU/mL)</th>
<th>EP5-T2 Calculated Point Estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serum Control 1</td>
<td>1</td>
<td>80</td>
<td>66.9</td>
<td>2.56 3.83</td>
</tr>
<tr>
<td>Within-run</td>
<td>Serum Control 2</td>
<td>1</td>
<td>80</td>
<td>220.8</td>
<td>3.15 1.43</td>
</tr>
<tr>
<td>Total</td>
<td>Serum Control 1</td>
<td>1</td>
<td>80</td>
<td>66.9</td>
<td>2.79 4.17</td>
</tr>
<tr>
<td></td>
<td>Serum Control 2</td>
<td>1</td>
<td>80</td>
<td>220.8</td>
<td>3.72 1.68</td>
</tr>
</tbody>
</table>

<sup>a</sup> The point estimate is based on the pooled data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer’s instructions.

**NOTICE**

These degrees of precision and equivalency were obtained in typical testing procedures on a SYNCHRON LX® System and are not intended to represent the performance specifications for this reagent.

**ADDITIONAL INFORMATION**

For more detailed information on SYNCHRON LX Systems or UniCel DxC Systems, refer to the appropriate system manual.

**SHIPPING DAMAGE**

If damaged product is received, notify your Beckman Coulter Clinical Support Center.
REFERENCES


**Beckman Coulter Ireland Inc., Mervue Business Park, Mervue, Galway, Ireland (353 91 774068)**

**Beckman Coulter, Inc., 250 South Kraemer Blvd., Brea, CA 92821**