INTENDED USE
Rapid latex agglutination test for the qualitative and semi-quantitative
determination of Rheumatoid Factor (anti-gamma globulin).

SUMMARY AND EXPLANATION
Rheumatoid arthritis is a chronic systemic disease of unknown etiology. It is
frequently characterized by swelling and pain in the joints and by inflammatory
and degenerative processes involving cartilage, synovial membrane or muscle
tissue. The disease is widespread in the United States and throughout the
world, and is found in all age groups. Most typically, its onset is in young adults
in their thirties and forties. While no specific cure has yet been found, early
therapy is of great value in halting or minimizing irreversible damage to the
joints. For this reason prompt diagnosis is of great importance.

A characteristic of rheumatoid arthritis is the presence in the blood and in
synovial fluid of a reactive group of proteins called Rheumatoid Factor. These
are macroglobulins having a molecular weight of 1 million. In the opinion of
many investigators, the Rheumatoid Factors are antibodies directed against
"altered" human gamma globulins. The Rheumatoid Factors are found in
70-100% of cases of definite rheumatoid arthritis depending on the test
procedure used to detect them. Because of this widespread incidence of RF,
its demonstration is a useful laboratory criterion for the diagnosis of suspected
rheumatoid arthritis. By comparison the occurrence of RF in arthritis or
rheumatic fever is less than 2 and 3% respectively. It should be noted that
incidence of RF have been reported in a variety of nonrheumatic diseases
such as pulmonary tuberculosis, bacterial endocarditis and syphilis as well as
others. A significant incidence of RF in the aged has also been observed.

Since the discovery of RF, there have been many techniques developed to
identify and quantitate these factors. The most generally useful techniques
have been agglutination procedures employing polystyrene particles coated
with a layer of absorbed human gamma globulin. The RF present in a test
serum reacts with the coating material causing a visible agglutination of the
inert latex particles. It is this reaction which is the basis of the CENOGENICS'
RF TEST.

CENOGENICS' RF TEST SET for the detection of Rheumatoid Factors rapidly
and accurately identifies the presence of RF, one of the criteria for the diagnosis
of rheumatoid arthritis.

In the presence of Rheumatoid Factor positive antiserum, CENOGENICS' latex-globulin RF reagent can be used to demonstrate agglutination both
qualitatively and quantitatively.

PRINCIPLES OF THE PROCEDURE
The principle of the test is an immunologic reaction between the Rheumatoid
Factor (RF), a macromolecular molecule globulin found in serum and the
corresponding IgG coated onto finely dispersed polystyrene latex particles.

CLIA COMPLEXITY: Moderate
REAGENTS
RF LATEX DIRECT REAGENT: polystyrene latex particles coated with human IgG and suspended in a glycine buffer.

POSITIVE CONTROL SERUM: a stabilized human serum containing rheumatoid factors reactive with the latex reagent.

NEGATIVE CONTROL SERUM: a stabilized human serum nonreactive with the latex reagent.

Note: All reagents are preserved with sodium azide (1mg/ml).

SENSITIVITY
8 IU/ml with a tolerance of 6-16 IU/ml calibrated against the WHO International RA standard.

MATERIALS PROVIDED WITH TEST SET
1. RF Latex Direct Reagent
2. Positive Control Serum
3. Negative Control Serum
4. 6-Well Test Slide
5. Disposable Pipettes
6. Product Instructions

MATERIALS REQUIRED BUT NOT PROVIDED
1. Test Tubes (for quantitative method)
2. Serological Pipettes
3. Laboratory Timer
4. Laboratory Rotator (optional)
5. Isotonic Saline (0.85% sodium chloride, for quantitative method)

STORAGE CONDITIONS
Store at 2° - 8°C.

STABILITY
Expiration date is specified on the label. Biological indication of product instability is evidenced by inappropriate reaction of the latex reagent with the corresponding positive and negative controls.

PRECAUTIONS
1. For invitro diagnostic use.
2. Do not use beyond the expiration date.
3. Handle all specimens of human origin as if capable of transmitting disease.
4. The reagents in this kit contain sodium azide. Sodium azide may react with lead and copper plumbing to form highly explosive metal oxides. Upon disposal, flush with large volume of water to prevent oxide build up.

REAGENT PREPARATION
No reagent preparation is required. Reagents are ready to use.

SPECIMENS
This test should be performed on fresh serum. The samples may be stored refrigerated (2° - 8°C) for a maximum of 7 days. If longer storage is required, store at -20°C. Heavy bacterial contamination may cause positive agglutination. Markedly lipemic sera should not be tested because of the possibility of nonspecific reactions.
TEST PROCEDURE (METHOD I, QUALITATIVE)
1. Bring all reagents and specimens to room temperature.
2. Shake the latex reagent gently, expel the contents of the dropper and refill.
3. Deliver on drop (50 µl) of patient sample to a circle on the test slide. Use a new pipet for each sample.
4. Using the dropper provided, place a drop of the latex reagent next to each specimen on the test slide.
5. Mix each specimen and latex with a disposable stirrer and spread over the entire surface of each circle.
6. Rotate the slide (80 - 100 r.p.m.) for 2 minutes.
7. Examine under a bright light source for the presence of agglutination.

RESULTS
POSITIVE: Agglutination (clumping of the latex particles) indicates a positive result. A weakly reactive serum produces a very fine granulation or partial clumping.
NEGATIVE: The absence of agglutination indicates a negative result.

QUALITY CONTROL
Positive and negative controls should be tested with each series of test sera. The controls supplied by CENOGENICS are to be used exactly as outlined in steps 1 thru 4 above without further dilution.

A positive control will produce coarse agglutinated flocs. A negative control will produce no agglutination. It should be used as a basis for comparison. The relative degree of smoothness of the reagent itself should be considered and incorporated in reading the results.

If the indicated results, using the positive and negative controls are not obtained, the RF Latex Kit should not be used.

TEST POSITIVE (METHOD II, SEMIQUANTITATIVE)
1. Using isotonic saline (0.85% sodium chloride), prepare a serial dilution of the serum starting at 1:2 thru 1:64.
2. Test each dilution as described in the Qualitative Procedure.

RESULTS
The titer is reported as the reciprocal of the highest dilution which gives a visible agglutination.

LIMITATIONS OF THE PROCEDURE
The detection limit of the CENOGENICS' RF Latex Direct Test is 8 IU/ml. In a comparison study between the CENOGENICS' RF Latex Direct Test and a commercially available product, the agreement was 98.8%.

EXPECTED VALUES AND PERFORMANCE CHARACTERISTICS
The clinical significance of RF determination consist in differentiation between rheumatoid arthritis, in which the rheumatoid factor has been demonstrated in the serum of approximately 80% of the cases examined and rheumatic fever in which the rheumatoid factor is almost always absent. The RF is more frequently positive in active processes of greater duration than in diseases which are less active or are still in early stages.

It is occasionally found in the serum of patients with polyarthritis nodosa, systemic lupus erythematosus and a variety of chronic inflammatory illnesses such as tuberculosis, leprosy, syphilis and bacterial endocarditis. Sera tested
from these related diseases showed positive reactions in approximately 6% of tested cases.

Approximately 3.5% of known rheumatoid patients do not react in the screening test, on the other hand, 2% of sera from apparently healthy individuals gave RF reaction.

INTERFERING SUBSTANCES
The following substances, at the concentrations listed below, were added to serum specimens and found to have no effect in the assay results:

<table>
<thead>
<tr>
<th>Substance</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin</td>
<td>0.5 to 20 mg/dl</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>0.63 to 10 g/l</td>
</tr>
<tr>
<td>Lipids</td>
<td>0.63 to 10 g/l</td>
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REFERENCES