1. INTENDED USE
The kit has been designed for the quantitative determination of Rubella IgM in human serum. The method can be used for samples over the range of 0-30 AU/ml. The test has to be performed on the Maglumi fuly auto analyzer (including Maglumi 1000, Maglumi 2000, Maglumi 2000 plus).

2. SUMMARY AND EXPLANATION OF THE TEST
Rubella is a viral exanthematous infectious disease caused by rubella virus, a single-stranded RNA virus belonging to the Togavirus group. The illness follows a typically benign clinical course with rare complications and is subclinical in a large proportion of cases. Symptomatology is generally mild, characterized by fever, malaise, a maculopapular rash of three to five days duration and, possibly, coryza and conjunctivitis. The disease is usually accompanied by lymphadenopathy. Infection confers lifelong immunity.

Infection from rubella virus is particularly disastrous if contracted during the first four months of gestation. If not immunologically protected, women infected during pregnancy run a high risk of embryofetal damage. Congenital rubella causes a wide range of severe defects, many of which are permanent and adversely affect later development (cataract, deafness, hepato-splenomegaly, psychomotor retardation, bone alterations, cardiopathies, neuropathies). Pathological consequences on the foetus or newborn depend on teratogenity of the virus and on the time of pregnancy when the infection has been contracted. Gestational age at the time of maternal infection is considered the most important determinant of intrauterine transmission and foetal damage. It is generally accepted that the risk decreases with increasing gestational age: it is highest in case of infection during the first two months of pregnancy (40-60%) and progressively decreases during the fourth and fifth months (10-20%).

Clinical findings in newborns and virus isolation studies have demonstrated that foetal infection is rare be-yond the second trimester of gestation. Rubella virus is transmitted in utero during the course of primary maternal infection, whether apparent or inapparent, when the virus in the bloodstream infects the placenta and, subsequently, the foetus. Intrauterine transmission of virus associated with maternal reinfection is extremely rare, indicating that maternal immunity (whether naturally derived or vaccine-induced) protects against intrauterine infection. Maternal infection may result in (a) no infection of the embryo; (b) resorption of the embryo (seen only with infections occurring in the earliest stages of gestation); (c) miscarriage; (d) stillbirth; (e) infection of placenta without foetal involvement or (f) infection of both the placenta and foetus. Infected infants may present obvious multiple organ involvement or, as is frequently observed, no immediately evident disease. However, after long-term follow-up, many of these seemingly unaffected infants have evidence of hearing loss, or central nervous system lesions, or other defects.

The first humoral immune response to infection is the synthesis of specific anti-rubella virus IgM antibody which reaches high serum levels two weeks after the rash and lasts in the circulation for one to two months. Specific IgG antibody generally appears a few days after the onset of rash, about one week after IgM develops. It rapidly increases to reach a plateau six to ten weeks after the onset of symptoms and then progressively decreases to a level (15-200 IU/mL) lasting for the whole life. Reinfection, completely asymptomatic, is accompanied by moderately increased levels of specific IgG.

Correct detection of IgM and IgG antibodies to rubella virus provides an essential tool for diagnosing and following up acute infection, for assessment of immune status in fertile women, and therefore for adopting suitable prophylaxis in susceptible women of child-bearing age. Since when a vaccine was made available, the assay of IgG to rubella virus has been widely used to determine seroconversion of the recipient after vaccination.

3. PRINCIPLE OF THE TEST
Sandwich immunoluminometric assay:
Mouse anti-human IgM is used to label ABEI, and use purified Rubella antigen to coat nano magnetic microbeads. Sample, Calibrator or Control, Buffer, and nano magnetic microbeads coated with Rubella antigen are mixed thoroughly and incubated at 37°C and cycle washing for 1 time. Then add ABEI Label, incubation and form a sandwich, then washing for the 2nd time. Subsequently, the starter reagents are added and a chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as RLU within 3 seconds and is proportional to the concentration of Rubella IgM present in controls or samples.

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**FOR PROFESSIONAL USE ONLY**

Store at 2...8 °C

**SYMBOLS USED ON LABELS**

- Authorized Representative in Europe
- Manufacturer
- Attention. See Instructions For Use
- Contents of kit
- In vitro diagnostic medical device (In vitro diagnostic use)
- Lot number
- Catalogue Code
- Expiry date (Use by...)
- Temperature limitation (store at 2...8 °C)
- Number of tests
- Keep away from sunlight
- Biological risks

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4. KIT COMPONENTS

4.1 Material supplies

<table>
<thead>
<tr>
<th>Reagent Integral for 100 determinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nano magnetic microbeads: TRIS buffer, 1.2% (W/V), 0.2% NaOH, coated with Rubella antigen</td>
</tr>
<tr>
<td>Calibrator low</td>
</tr>
<tr>
<td>Calibrator high</td>
</tr>
<tr>
<td>Buffer</td>
</tr>
<tr>
<td>ABEI Label: Mouse anti-human IgM labeled ABEI contains BSA, 0.2% NaOH</td>
</tr>
<tr>
<td>Diluent</td>
</tr>
</tbody>
</table>

*All reagents are provided ready-to-use.

*Please prepare 0.9% sodium chloride solution in case of insufficient diluents.

Accessories required but not provided

- Maglumi Reaction module
- Maglumi Starter Kit 1+2
- Maglumi Light check
- Maglumi Wash/System Liquid

4.2 Preparation of the Reagent Integral

Before the sealing is removed, gentle and careful horizontal shaking of the Reagent Integral is essential (avoid foam formation!). Remove the sealing and turn the small wheel of the magnetic microbeads compartment to and fro, until the colour of the suspension has changed into brown. Place the Integral into the reagent area and let it stand there for 30 mins. During this time, the magnetic microbeads are automatically agitated and completely resuspended.

NOTE: Do not interchange Nano Magnetic Microbeads from different reagents!

4.3 Storage of the Reagents Integral

- Sealed: Stored at 2-8°C until the expiry date.
- Opened: Stable for 4 weeks. After this period, it is still possible to keep on using the Reagent Integral provided that the controls are found within the expected ranges.
- Keep upright for storage.
- Keep away from direct sunlight.

5. Origin of Calibrators

Calibrators in the Reagent Kit are from Fitzgerald.

Biological root: recombinant protein, with a purity ≥ 99%. No HBsAg, anti-HCV, and anti-HIV is found.

6. Calibration

6.1 2 point recalibration

Via the measurement of calibrators, the predefined master curve is adjusted (recalibrated) to a new, instrument-specific measurement level with each calibration.

6.2 Frequency of Recalibration

- After each exchange of lot (Reagent Integral or Starter Reagents).
- Every week and/or each time a new Integral is used (recommendation).
- After each servicing of the Maglumi Fully Auto analyzer.
- If controls are beyond the expected range.
- Room temperature changes exceed 5°C (recommendation).

7. Sample Collection, Material and Storage

- Collect samples using standard procedures.
- Sample material: serum.
- Store at 2-8°C: 24 hours.
- For longer storage periods: freeze to below -20°C.
- Avoid repeated freezing and thawing cycles.
- Stored samples should be thoroughly mixed prior to use (Vortex mixer).
- Vacuum tubes
  (a) Blank tubes are recommended type for collecting samples.
  (b) If plasma sample is needed, EDTA tube is conform to has no effect on the results.
  (c) Lithium heparin Sodium tube is found to increase the sample RU and cause test results deviation.
  (d) Please ask SNIBE for advice if special additive must be used in the sample blood.

8. WARNING AND PRECAUTIONS FOR USERS

- For use in IN-VITRO diagnostic procedures only.
- Do not interchange reagents from different lots. Do not use kit components beyond their labelled expiry date.
- All samples, biological reagents and materials used in the assay must be considered potentially able to transmit infectious agents. They should therefore be disposed of in accordance with the prevailing regulations and guidelines of the agencies holding jurisdiction over the laboratory, and the regulations of each country. Disposable materials must be incinerated; liquid waste must be decontaminated with sodium hypochlorite at a final concentration of 5% for at least half an hour. Any materials to be reused must be autoclaved using an overkill approach (USP 24,2000,p.2143). A minimum of one hour at 121°C is usually considered adequate, though the users must check the effectiveness of their decontamination cycle by initially validating it and routinely using biological indicators.
- The calibrators in this kit are prepared from bovine serum products. However, because no test method can offer complete assurance that HIV, Hepatitis B Virus or other infectious agents are absent, these reagents should be considered a potential biohazard and handled with the same precautions as applied to any serum or plasma specimen.

9. Test Procedure

To ensure proper test performance, strictly adhere to the operating instructions of the Maglumi Fully Auto analyzer. Each test parameter is identified via a RFID tag on the Reagent Integral. For further information please refer to the Maglumi Fully Auto Operator’s Manual.

10. Quality Control

- Observe quality control guidelines for medical laboratories.
- Use suitable controls for in-house quality control.

11 Results

11.1 Calculation of Results

- The analyzer automatically calculates the Rubella IgM concentration in each sample by means of a calibration curve which is generated by a 2-point calibration master curve procedure. The results are expressed in AU/ml. For further information please refer to the Maglumi Fully Auto Operator’s Manual.

11.2 Interpretation of Results

- Reference values: < 2AU/ml.
- Results may differ between laboratories due to variations in population and test method. Each laboratory should establish its own reference range.

12. Limitations of the procedure

12.1 Use Rubella IgM value as a kind of auxiliary material for other testing data when in diagnosis. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.

A skillful technique and strict adherence to the instructions are necessary to obtain reliable results. Bacterial contamination of samples or repeated freeze-thaw cycles may affect the test results. Assay results should be utilized in conjunction with other clinical and laboratory data to assist the clinician in making individual patient management decisions.

13. Performance Characteristics

13.1 Accuracy

Consider calibrator high of known concentration as a sample, dilute it by 1/2 ratio with diluent, and measure its diluted concentration for 10 times. Then calculate the recovery of measured concentration and expected concentration. The recovery should be within 90%-110%.

13.2 Precision

Intra-assay coefficient of variation was evaluated on Calibrator High repeatedly measured 10 times in the same assay, calculating their coefficient of variation, the results should <10%.

Inter-assay coefficient of variation was evaluated on three batches of kit, repeatedly measured 10 times of Calibrator High, calculating three batches of kit for Calibrator High between the measured values of the coefficients of variation, the results should <15%.

13.3 Sensitivity

The sensitivity is defined as the concentration of Rubella IgM equivalent to the mean RU of 20 replicates of the zero standard plus two standard deviations
corresponding to the concentration from the standard curve. The sensitivity is typically less than 0.01 AU/ml.

13.4 Specificity
The specificity of the Rubella IgG assay system was assessed by measuring the apparent response of the assay to various potentially cross reactive analytes.

When TOXO IgG=30AU/ml, CMV IgG=30AU/ml, the detection of Rubella IgM is less than 1 AU/ml.

13.5 Linearity
Conduct a logarithmic transform to the RLU value and concentration value of 6 Calibrators. After a double logarithmic fitting, the absolute value of its linearity should exceed 0.9800.

14. References