



**WHO International Standard
Anti Rubella Immunoglobulin, Human
NIBSC code: RUBI-1-94
Instructions for use
(Version 9.0, Dated 04/05/2020)**

1. INTENDED USE

This material has been prepared and characterised by the Statens Serum Institut (SSI), Copenhagen, Denmark. With effect from 1st July 1997, the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK is the custodian and distributor of this material. The package insert from SSI is shown on the last two pages of this document.

IVD manufacturers, regulators and assay users should be made aware of RUBI-1-94 potential lack of commutability when used as a calibrant. This was highlighted by the WHO Expert Committee on Biological Standardization in TRS 68th Report (Section 3.3.4: 2018).

RELEVANT INFORMATION

For details of this International Standard, please refer to the enclosed package insert from the Statens Serum Institut (prepared in 1995) which describes the preparation as the proposed 3rd international standard preparation for anti-rubella serum, human.

The unpublished report of the 47th meeting of the WHO Expert Committee on Biological Standardization in 1996 contains the following explanation: "The Committee noted the confused nomenclature that had arisen when the first International Reference Preparation of Anti-Rubella Serum, Human (a serum) was replaced by the second (a preparation of normal immunoglobulin) and decided to take the necessary corrective action on replacement of the latter. In view of the results of the collaborative study, the Committee established the preparation coded RUBI-1-94 as the first International Standard for Anti-Rubella Immunoglobulin, Human and assigned a potency of 1600 International Units to the contents of each vial".

The first sentence of section 3 (Use of the Standard) in the enclosed package insert from the Statens Serum Institute should be disregarded

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The preparation contains material of human origin, and either the final product or the source materials, from which it is derived, have been tested and found negative for HBsAg, anti-HIV and HCV RNA.

The ampouled material has been tested and found negative for HBsAg and anti-HIV, and HCV RNA not detectable by PCR. However, As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

3. UNITAGE

1600 International Units (IU) per vial

4. CONTENTS

Country of origin of biological material: Denmark.

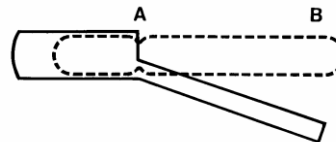
5. STORAGE

Unopened vials should be stored at -20°C or below

Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

Tap the ampoule gently to collect the material at the bottom (labelled) end. Ensure ampoule is scored all round at the narrow part of the neck, with a diamond or tungsten carbide tipped glass knife file or other suitable implement before attempting to open. Place the ampoule in the ampoule opener, positioning the score at position 'A'; shown in the diagram below. Surround the ampoule with cloth or layers of tissue paper. Grip the ampoule and holder in the hand and squeeze at point 'B'. The ampoule will snap open. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.



Side view of ampoule opening device containing an ampoule positioned ready to open. 'A' is the score mark and 'B' the point of applied pressure.

7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution

Dissolve the total contents of the ampoule in a known volume of physiological saline or any other suitable diluent. The solution will contain 1600 International Units per ampoule.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

Not applicable

10. ACKNOWLEDGEMENTS

Not applicable

11. FURTHER INFORMATION

Further information can be obtained as follows;

This material: enquiries@nibsc.org

WHO Biological Standards:

<http://www.who.int/biologicals/en/>

JCTLM Higher order reference materials:

<http://www.bipm.org/en/committees/jc/jctlm/>

Derivation of International Units:

http://www.nibsc.org/standardisation/international_standards.aspx

Ordering standards from NIBSC:

<http://www.nibsc.org/products/ordering.aspx>

NIBSC Terms & Conditions:

http://www.nibsc.org/terms_and_conditions.aspx

12. CUSTOMER FEEDBACK

Customers are encouraged to provide feedback on the suitability or use of the material provided or other aspects of our service. Please send any comments to enquiries@nibsc.org



13. CITATION

In all publications, including data sheets, in which this material is referenced, it is important that the preparation's title, its status, the NIBSC code number, and the name and address of NIBSC are cited and cited correctly.

14. MATERIAL SAFETY SHEET

Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

Physical and Chemical properties	
Physical appearance: Freeze-dried powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains dried material of human origin
Toxicological properties	
Effects of inhalation:	Not established. Avoid ingestion
Effects of ingestion:	Not established. Avoid ingestion
Effects of skin absorption:	Not established. Avoid ingestion
Suggested First Aid	
Inhalation:	Seek medical advice
Ingestion:	Seek medical advice
Contact with eyes:	Wash with copious amounts of water. Seek medical advice
Contact with skin:	Wash thoroughly with water.
Action on Spillage and Method of Disposal	
Spillage of ampoule contents should be taken up with absorbent material wetted with an appropriate disinfectant. Rinse area with an appropriate disinfectant followed by water. Absorbent materials used to treat spillage should be treated as biological waste.	

15. LIABILITY AND LOSS

In the event that this document is translated into another language, the English language version shall prevail in the event of any inconsistencies between the documents.

Unless expressly stated otherwise by NIBSC, NIBSC's Standard Terms and Conditions for the Supply of Materials (available at http://www.nibsc.org/About_Us/Terms_and_Conditions.aspx or upon request by the Recipient) ("Conditions") apply to the exclusion of all other terms and are hereby incorporated into this document by reference. The Recipient's attention is drawn in particular to the provisions of clause 11 of the Conditions.

16. INFORMATION FOR CUSTOMS USE ONLY

Country of origin for customs purposes*: Denmark * Defined as the country where the goods have been produced and/or sufficiently processed to be classed as originating from the country of supply, for example a change of state such as freeze-drying.
Net weight: 0.1g
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable.
Attached: No

17. CERTIFICATE OF ANALYSIS

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

NIBSC does not provide a Certificate of Analysis for WHO Biological Reference Materials because they are internationally recognised primary reference materials fully described in the instructions for use. The reference materials are established according to the WHO Recommendations for the preparation, characterization and establishment of international and other biological reference standards http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biol_efstandardsrev2004.pdf (revised 2004). They are officially endorsed by the WHO Expert Committee on Biological Standardization (ECBS) based on the report of the international collaborative study which established their suitability for the intended use.



WHO International Laboratory for Biological Standards

Phone: +45 32 68 34 66 (G.A. Hansen direct)
Telefax: +45 32 68 31 50 (Laboratory direct)
E-mail (Internet): GAHANSEN@STANDARD.SSI.DK



STATENS
SERUM
INSTITUT
*prevention and control
of infectious diseases
and congenital disorders*

Proposed

**INTERNATIONAL STANDARD
for
ANTI-RUBELLA SERUM, HUMAN
(proposed 3rd international standard preparation)**

1. THE STANDARD PREPARATION

The second International Standard for Anti-Rubella Serum, Human was established in 1970. Despite of the name this preparation consisted of ampoules each containing the freeze-dried residues of 2 ml of a mixture of normal human immunoglobulin and an equal volume of saline. An International Unit for Anti-Rubella Serum was defined as the activity contained in 0.14595 mg of the dry material in the ampoule.

The demand for the second International Standard for Anti-Rubella Serum, Human has particularly in later years, been high and the stocks are almost depleted. An interim stop for the distribution of this preparation has therefore been in force since primo 1995. The remaining ampoules will be needed for arranging the replacement and for future reference purposes.

In the interim period until a replacement preparation has been finally established, laboratories may, if needed, obtain the proposed replacement for calibration purposes.

The WHO Expert Committee for Biological Standardization noted at its 45th meeting in 1995 that "following the recognition of the need for a replacement for the second International Reference Preparation of Anti-Rubella Serum, Human, which was prepared from normal human immunoglobulin (WHO Technical Report Series No. 848, 1994 p.10), a new preparation of normal human immunoglobulin had been obtained (BS/94.1762). The Committee was informed, that this preparation will be proposed as a replacement preparation for the second International Reference Preparation of Anti-Rubella Serum, Human, and that a limited collaborative assay will be arranged".

The proposed replacement preparation (code RUBI-1-94) consist of vacuum sealed vials each containing the freeze-dried residues of 2 ml of a mixture of normal human immunoglobulin and an equal volume of sterile distilled water. Each vial is after freeze-drying controlled for vacuum by high frequency testing and individually packed in vacuum sealed plastic bags.

2. AMPOULE CONTENTS

Preliminary estimates of potency and stability of the proposed replacement preparation RUBI-1-94 have indicated the preparation to be a suitable replacement.

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Statens Serum Institut
5 Artillerivej
2300 Copenhagen S
Denmark

Tel.: +45 3268 3268
Fax: +45 3268 3868
E-mail: serum@ssi.d



An international collaborative study to calibrate the proposed replacement (RUBI-1-94) against the second International Standard for Rubella Serum, Human has been carried out in 11 laboratories in 7 countries using both Immunoassays methods and Hemagglutination Inhibition Test. This study has almost been completed. Based on results obtained from 9 laboratories in 7 countries using both methods potency of RUBI-1-94 is estimated to 1600 International Units (IU) of Anti-Rubella Serum, Human for the total content of an ampoule.

3. USE OF THE STANDARD

A solution of the total contents of an ampoule will contain 1700 IU in the total volume. The ampoule might be reconstituted in physiological saline or any other suitable diluent. After reconstitution the solution of the standard must preferably be used at once for calibrating working standards unless a validated procedure for storage is used.

Many laboratories have, however, experienced difficulties by calibrating their own working standards. Thus the proposed third International Standard for Anti-Rubella Serum, Human can be requested also as working standard.

The use of an immunoglobulin preparation as a reference material for diagnostic assays of human sera in clinical diagnostic laboratories is not an ideal solution. Therefore work has been going on for some time to prepare reference materials both from acute phase sera with high contents of rubella IgM antibodies and low avidity rubella IgG antibodies as well as from convalescent sera with high avidity IgG antibodies. These two new reference preparations for rubella IgM antibodies and rubella IgG antibodies are intended to replace the immunoglobulin preparation in few years.

5. WARNING

International reference materials of human origin might constitute a risk in regard to transmission of blood borne infections. All samples should therefore be treated as if capable of causing infection.

It should also be noted that distribution of international reference materials is being performed as a public service. Consequently, by accepting delivery and proceeding to use the reference material concerned, the recipient agrees not to hold the Statens Seruminstitut, Copenhagen or WHO liable for the consequences of any injury or illness attributable to infection acquired from the reference material.

If a recipient does not agree to this condition on use of the reference materials, he must immediately return the reference material to the Statens Seruminstitut, Copenhagen.

4. GENERAL REMARKS ABOUT INTERNATIONAL REFERENCE MATERIALS

International biological standards and international biological reference reagents provide a means of ensuring uniformity throughout the world in the designation of the potency or activity of preparations used in the prophylaxis, therapy, or diagnosis of disease, where this cannot be expressed in terms of physical or chemical quantities. The International Units are units of quantities of "effective constituent"

The standard is the material as it exists in the ampoules; the "material" thus includes the effective constituents together with all the other constituents that may be present (moisture, carrier, buffer, salt etc., according to the form in which the standard is available).

International biological reference materials are intended for use in the calibration of the contents of "effective constituent" in national or working standard preparations and for the expression of these contents in the respective International Units. For the routine use in the laboratory the national or working standards should preferably be used. A handling charge will be claimed for distribution of international reference materials to other than national control laboratories.