



**WHO International Standard
1st International Standard for Antiserum to Respiratory Syncytial
Virus**

**NIBSC code: 16/284
Instructions for use
(Version 4.0, Dated 01/04/2020)**

1. INTENDED USE

This preparation was established by the WHO Expert Committee on Biological Standardization in 2017 as the 1st International Standard for antiserum to respiratory syncytial virus. It was shown to be suitable for the standardization of virus neutralization methods to measure antibody levels against RSV/A in human sera.

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. 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

1,000 International Units (IU) of anti-RSV/A neutralizing antibodies per ampoule.

1,000 International Units (IU) of anti-RSV/B neutralizing antibodies per ampoule.

4. CONTENTS

Country of origin of biological material: United States.
Each ampoule contains the freeze dried residue of 0.5 ml human serum. The candidate standard has been prepared from a bulk of human sera. 0.5 ml aliquots of this bulk were filled in DIN ampoules and freeze dried at NIBSC following documented procedures. This fill was 0.5g fill weight with a mean dry weight of 0.043g. The coefficient of variation (CV) was 0.27%. Residual moisture measured on 12 samples gave a mean of 1.04% with a CV of 25.50% and oxygen measured in the headspace of 12 ampoules, gave a mean of 0.44% with a CV of 26.02%.

5. STORAGE

The ampoules should be stored at -20°C or below until use.

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

6. DIRECTIONS FOR OPENING

DIN ampoules have an 'easy-open' coloured stress point, where the narrow ampoule stem joins the wider ampoule body. Various types of ampoule breaker are available commercially. To open the ampoule, tap the ampoule gently to collect material at the bottom (labelled) end and follow manufactures instructions provided with the ampoule breaker.

7. USE OF MATERIAL

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

Ampoules should be reconstituted on the day of the assay by adding exactly 0.5 ml of pure sterile distilled water to give 2000 IU/mL. Shake gently without the formation of foam to ensure that all contents are

reconstituted. To remove the reagent from the ampoule it is necessary to use some form of transfer pipette rather than a volumetric pipette. The contents of the ampoules should not be assumed to be sterile.

Calibration of In-House Reference Standard:

In-house serum selected for possible reference purposes and the International Standard for Antiserum to RSV should be titrated in parallel on at least 6 separate occasions using at least 3 replicates per serum dilution.

A GMT for both the reference serum and the international standard should be calculated from the 6 assays and plugged into the following equations to determine IU or IU/mL.

IU Reference Standard = (GMT Reference / GMT International Standard) * Assigned potency of International standard

IU/mL Reference Standard = GMT Reference / (GMT International Standard / Assigned potency of International Standard/mL)

Example:

GMT of in-house reference = 1500

GMT of International Standard Antiserum = 1145

Assigned potency of International Standard Antiserum = 1000 / vial or 2000 / mL

Therefore:

Potency of in-house reference (IU/mL) = 1500 / (1145 / 2000) = 2620.1 IU/mL

Potency of in-house reference (IU) = (1500 / 1145) * 1000 = 1310.5 IU

GMT = Geometric Mean titre

8. STABILITY

It is the policy of WHO not to assign an expiry date to their international reference materials. They remain valid with the assigned potency and status until withdrawn or amended.

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

Users should determine the stability of the material according to their own method of preparation, storage and use. Multiple freeze/thaw cycles should be avoided.

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

9. REFERENCES

1. McDonald, J.U., et al., Establishment of the first WHO International Standard for antiserum to Respiratory Syncytial Virus: Report of an international collaborative study. *Vaccine*, 2018. 36(50): p. 7641-7649.

2. McDonald, J.U., et al., Report on the WHO collaborative study to establish the 1st International Standard for antiserum to Respiratory Syncytial Virus. WHO Expert Committee on Biological Standardisation, TRS 1011, 2017.

3. McDonald, J.U. et al., Expansion of the 1st WHO international standard for antiserum to respiratory syncytial virus to include neutralisation titres against RSV subtype B: An international collaborative study. *Vaccine*, 2019.

3. McDonald, J.U. et al., Update on the WHO collaborative study to establish the 1st International Standard for antiserum to Respiratory Syncytial Virus.

https://www.who.int/biologicals/expert_committee/BS.2019.2372_RSV_B_1st_IS_Report_FINAL.pdf



10. ACKNOWLEDGEMENTS

We would like to acknowledge PATH for donating the source material used to produce this standard and for funding the project that led to its production.

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 and has a small white/yellowish cake	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify): Contains material of human origin	
Toxicological properties	
Effects of inhalation:	Not established, avoid inhalation
Effects of ingestion:	Not established, avoid ingestion
Effects of skin absorption:	Not established, avoid contact with skin
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*: United Kingdom
* 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: 0.5g
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable.
Attached: No

17. CERTIFICATE OF ANALYSIS

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_standardsrev2004.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.