



**WHO International Standard**  
**Third WHO International Standard for Anti-Rabies**  
**Immunoglobulin**  
**NIBSC code: 19/244**  
**Instructions for use**  
**(Version 1.0, Dated 09/12/2022)**

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### 1. INTENDED USE

This material serves as the primary biological standard for Rabies Immunoglobulin. The intended use of the International Standard is for the calibration and harmonisation of serological assays detecting neutralising antibodies against Rabies virus via focus inhibition test (RFFIT) and fluorescent antibody virus neutralisation (FAVN), as well as binding antibodies via ELISA.

### 2. CAUTION

**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. This preparation is not for administration to humans or animals**

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

The assigned potency of the Third WHO International Standard for anti-Rabies immunoglobulin is 164 IU/ampoule for RFFIT and FAVN assays. For measuring binding antibodies via ELISA the assigned potency is 128 IU/ampoule.

Uncertainty: the proposed unitage does not carry and uncertainty associated with its calibration. The only uncertainty is therefore derived from the variability of the dry fill weight of the ampoule with is 0.46%.

### 4. CONTENTS

Country of origin of biological material: United Kingdom.  
Each ampoule contains the freeze-dried equivalent of 0.5 mL of Human Rabies Immunoglobulin (HRIG) drug substance (DS). The material was produced under Good Manufacturing Practices (GMP), with plasma units collected from vaccinated donors and met all manufacturing specifications.

### 5. STORAGE

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**

The contents of each ampoule should be reconstituted in 0.5 mL of sterile distilled water. Following additional of the distilled water, the material must be allowed to become fully reconstituted before use. End-users have found that it may take > 1 hour with agitation for the material to become fully reconstituted.

### 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.

The stability of International Standard when reconstituted has not been specifically determined. Therefore, it is recommended that the reconstituted material is for single use only. Should users wish to store reconstituted material, they should determine the stability of reconstituted material according to their own method of preparation, storage and use.

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

### 9. REFERENCES

Wilkinson et al., WHO Collaborative Study to Assess the Candidate 3rd International Standard for Rabies Immunoglobulin. 2022 WHO Expert Committee on Biological Standardization. WHO/BS/2022.2435

### 10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of the collaborative study participants; the rabies diagnostic reference laboratory for validation testing and stability testing; and the donors of the candidate HRIG and anti-rabies plasma packs. We thank Professor Susan M. Moore, Veterinary Medical Diagnostic Laboratory, University of Missouri, MO, USA for her expert guidance on the sourcing of the materials and comments on the draft report. We would also like to thank Lindsay Stone and Emma Summersgill, Division of Virology at NIBSC, for assisting in the processing of the source materials and the NIBSC team in Standards Production and Development for the production of the candidate standards and distribution of the study materials.

### 11. FURTHER INFORMATION

Further information can be obtained as follows;  
This material: [enquiries@nibsc.org](mailto: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](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](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](mailto: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	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other Material of human origin (specify):	
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](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

<b>Country of origin for customs purposes*:</b> 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.
<b>Net weight:</b> 0.5 g
<b>Toxicity Statement:</b> Toxicity not assessed
<b>Veterinary certificate or other statement</b> if applicable.
<b>Attached:</b> 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\\_1nter\\_biolefststandardsrev2004.pdf](http://www.who.int/bloodproducts/publications/TRS932Annex2_1nter_biolefststandardsrev2004.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.