



**WHO International Standard
7th International Standard for Rabies vaccine
NIBSC code: 16/204
Instructions for use
(Version 1.0, Dated 08/11/2018)**

1. INTENDED USE

The International Standard (IS) for rabies vaccine is used in the standardisation of rabies vaccines in NIH mouse potency tests and in in vitro assays for glycoprotein content. This material was prepared from a bulk of Vero cell-derived, Pitman Moore strain, produced by the same manufacturing process as the former 6th IS (07/162) and 5th IS (RAV). As for previous standards, the 7th IS contains human albumin as stabiliser. The candidate standard was calibrated in IU against the 6th International Standard in a collaborative study in which 16 laboratories from 12 countries assayed the candidate standard as blinded duplicates. Data sets were analysed for 10 NIH mouse potency tests, 9 ELISA and 6 single radial immunodiffusion (SRD) tests (1).

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

The unitage assigned to this material is as follows:

For use in NIH mouse potency tests, the unitage is 8.9 IU/ampoule (i.e. 8.9 IU/mL when reconstituted as directed in 1mL distilled water).

For use in ELISA for glycoprotein content, the unitage is 2.5 IU/ampoule. (i.e. 5.0 IU/mL when the contents are reconstituted as directed in 0.5mL distilled water).

For use in SRD for glycoprotein content, the unitage is 2.9 IU/ampoule. (i.e. 5.8 IU/mL when the contents are reconstituted as directed in 0.5mL distilled water).

4. CONTENTS

Country of origin of biological material: France.

Each ampoule contains the freeze dried residue of a 0.5 ml aliquot of a commercial rabies vaccine bulk containing inactivated Pitman Moore virus grown in Vero cells. The preparation was 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 0.5238 g with a % coefficient of variation (%CV) of 0.3255%; n=372. The residual moisture measured on 12 samples gave a mean of 0.4% with a %CV of 20.5%. The oxygen headspace measured in 12 ampoules gave a mean of 0.13% with a %CV of 81.37%.

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

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

For use in in vivo NIH mouse tests, reconstitute the contents of the ampoule in 1mL distilled water. The resultant preparation is 8.9 IU/mL.

For use in ELISA (rabies virus glycoprotein content), reconstitute the contents of the ampoule in 0.5 mL distilled water. The resultant preparation is 5.0 IU/mL. (i.e 2.5 IU/0.5 mL).

for use in SRD (rabies virus glycoprotein content), reconstitute the contents of the ampoule in 0.5 mL distilled water. The resultant preparation is 5.8 IU/mL. (i.e 2.9 IU/0.5 mL).

The ampoules should be shaken gently without the formation of foam to ensure that all contents are completely reconstituted. When a reconstitution volume of 0.5mL is used, the ampoule may be left at ambient temperature for 30 minutes to facilitate complete dissolution of the contents.

8. STABILITY

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

Accelerated thermal degradation assessment of the freeze-dried product indicates that the candidate 7th IS Rabies vaccine (NIBSC 16/204) is stable for long-term storage at -20 °C or lower showing a predicted loss of potency of 0.002% per year when stored at -20 °C. The material may be shipped at ambient temperature.

Stability studies on reconstituted material have not been undertaken.

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

9. REFERENCES

1) WHO Expert Committee on Biological Standardization report (Post-ECBS) WHO/BS/2018.2335 is available online.

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of the donor of the source materials and the collaborative study participants. We would also like to thank Paul Chamberlain and Lindsay Stone, Division of Virology at NIBSC, for initial work on the development and validation of the candidate standard and NIBSC Standards Production and Development for the production of NIBSC 16/204 and distribution of the study materials.

We also thank Ivana Knezevic of the WHO and the International Working Group of the European Partnership for Alternatives to Animal Testing (EPAA) for their support, guidance and advice.

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	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains human albumin
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: 0.5 g
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_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.