WHO International Standard
The 5th International Standard for RABIES VACCINE
NIBSC code: RAV
Instructions for use
(Version 5.0, Dated 21/02/2008)

1. INTENDED USE
This material was 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.

For details of this International Standard, please refer to the enclosed package insert from the Statens Serum Institut.
The preparation is labelled ‘International Standard for Rabies vaccine (Fifth International Reference Material).

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
Each ampoule of this preparation contains 16 International Units of rabies vaccine

This preparation has also been assigned a unitage of 10 International Units of rabies virus PM glycoprotein and 135 International Units of rabies virus PM ribonucleoprotein.

4. CONTENTS
Country of origin of biological material: United Kingdom. Please refer to the package insert from the Statens Serum Institut.

5. STORAGE
Ampoules should be stored at -20°C on receipt. 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. Tap the ampoule gently to collect the material at the bottom (labeled) end. Ensure that the disposable ampoule safety breaker provided is pushed down on the stem of the ampoule and against the shoulder of the ampoule body. Hold the body of the ampoule in one hand and the disposable ampoule breaker covering the ampoule stem between the thumb and first finger of the other hand. Apply a bending force to open the ampoule at the coloured stress point, primarily using the hand holding the plastic collar. Care should be taken to avoid cuts and projectile glass fragments that might enter the eyes, for example, by the use of suitable gloves and an eye shield. Take care that no material is lost from the ampoule and no glass falls into the ampoule. Within the ampoule is dry nitrogen gas at slightly less than atmospheric pressure. A new disposable ampoule breaker is provided with each DIN ampoule.

7. USE OF MATERIAL
No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution. Reconstitute the contents of each ampoule in 1ml of distilled water. Please refer to the package insert from the Statens Serum Institut for further information.

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. Please refer to the package insert from the Statens Serum Institut for further information.

9. REFERENCES

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

### 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 |

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WHO International Laboratory for Biological Standards, UK Official Medicines Control Laboratory

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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.

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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: 1g

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_biologicalstandardsrev2004.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.
The Expert Committee on Biological Standardisation\(^1\) was however informed, that there is a need for the standardization of tests for rabies virus glycoprotein and ribonucleoprotein, two constituents which appear to be of importance for the protective activity of Rabies vaccine. In order to follow up this need, but taking into consideration that glycoproteins and perhaps also ribonucleoproteins are to some degree strain-specific, and since the Fifth International Standard for Rabies Vaccine is derived from the WI strain of virus, the Committee also assigned

10 International Units of Rabies Virus DM-Glycoprotein and
155 International Units of Rabies Virus WI-Ribonucleoprotein to the contents of each ampoule of the standard preparation. These definitions refer to the total contents in the preparation including what is free and bound to the virus.

3. USE OF THE INTERNATIONAL STANDARD

As all other international standard preparations the International Standard for Rabies Vaccine is only available in very limited amounts. The standard preparation should not be used for routine use but is intended for the calibration of national or laboratory reference materials.

If one ml of a national reference material has an activity equal to that of the International Standard Preparation when the standard preparation has been reconstituted in 10 ml, then each ml of the national reference has an activity of 1.0 International Units. When comparisons are made between national standards and the International Standard Preparation due regard must be paid to the volume of fluid in which the preparations are reconstituted.

Example 1:

National reference material (NNM) reconstituted in one ml. International standard reconstituted in 1 ml which by definition has an activity of 16 IU (Now 155 International Units) when reconstituted preparation and it is found that the International standard is five times as active as the NNM.

The potency of the NNM is \( = 3.2 \text{ IU per ml.} \)

Example 2:

If the International Standard Preparation has been reconstituted in 3.2 ml (which gives a solution containing 5 IU/ml), and the activity of the NNM (reconstituted as in Example 1) is found to be 2.5 IU per ml, then the International standard is twenty times as active as the NNM.

The International Standard for Rabies Vaccine is held and distributed by:

WHO International Laboratory for Biological Standards
Statens Serum Institute
9, Arntzivsvej
DK-2300 Copenhagen S, DENMARK

4. GENERAL REMARKS ABOUT INTERNATIONAL REFERENCE MATERIALS

International Biological standard and international biological reference reagents provide a means of ensuring uniformity throughout the world in the designation of the potency of activity of preparations used in the prophylaxis, therapy, or diagnosis of diseases, where this cannot be expressed in terms of physical or chemical quantities. The International Standards, however, are still expressions of quantities of "effective constituent".