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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
<th>Corrosive</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical appearance: Freeze dried</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable:</td>
<td>Yes</td>
<td>Oxidising:</td>
</tr>
<tr>
<td>Hygroscopic:</td>
<td>No</td>
<td>Irritant:</td>
</tr>
<tr>
<td>Flammable:</td>
<td>No</td>
<td>Handling:</td>
</tr>
<tr>
<td>Other (specify):</td>
<td>Contains human albumin</td>
<td></td>
</tr>
</tbody>
</table>

Toxicological properties

<table>
<thead>
<tr>
<th>Effects of inhalation:</th>
<th>Not established, avoid inhalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects of ingestion:</td>
<td>Not established, avoid ingestion</td>
</tr>
<tr>
<td>Effects of skin absorption:</td>
<td>Not established, avoid contact with skin</td>
</tr>
</tbody>
</table>

Suggested First Aid

<table>
<thead>
<tr>
<th>Inhalation:</th>
<th>Seek medical advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingestion:</td>
<td>Seek medical advice</td>
</tr>
</tbody>
</table>
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**: 1g
- **Toxicity Statement**: Non-toxic
- **Veterinary certificate or other statement if applicable**: No
- **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生物科技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.
The Expert Committee on Biological Standardization 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 VN strain of virus the Committee also assigned:

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

2. 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 (NRM) reconstituted in one ml. International Standard reconstituted in 1 ml which by definition has an activity of 1.0 IU per ml. If 0.1 ml of the NRM when reconstituted has an activity of 0.1 IU/ml and it is found that the International standard is five times as active as the NRM, the potency of the NRM is

\[ \frac{1}{5} = 0.2 \text{ IU per ml.} \]

Example 2:
If the International Standard Preparation has been reconstituted in 3.2 ml (which gives a solution containing 3.2 IU/ml), and the activity of the NRM (reconstituted as in Example 1) is found to be 0.8 IU/ml, for a reconstituted international standard, then the potency of the NRM is

\[ 0.8 \times 5 = 4 \text{ IU/ml.} \]

The International Standard for Rabies Vaccine is held and distributed by the WHO International Laboratory for Biological Standards, Statens Serum Institute, B. Artillerivej, DK-2300 Copenhagen S, DENMARK.

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, however, are still expressions of quantities of "effective constituent".