WHO International Standard
Anti-tick borne encephalitis serum
NIBSC code: TISA
Instructions for use
(Version 5.0, Dated 30/04/2020)

1. INTENDED USE
This material has been 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.

The package insert from SSI is attached. (Please note that the statement in Section 2 of the SSI package insert about charges is no longer valid.)

2. CAUTION
This preparation is not for administration to humans or animals in the human food chain.

The material is not of human or bovine origin. 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
1ml reconstituted serum was found to neutralize 10⁷.⁷⁰ virus in experiments with intravenous injection of white mice (see SSI insert)

4. CONTENTS
Country of origin of biological material: United Kingdom.

5. STORAGE
Store unopened ampoules at -20°C

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

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.

9. REFERENCES
See Insert from SSI

10. ACKNOWLEDGEMENTS
NIBSC would like to thank SSI for the donation of this standard

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/tlm/
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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical appearance: Freeze-</td>
</tr>
<tr>
<td>Corrosive: No</td>
</tr>
<tr>
<td>dried powder</td>
</tr>
<tr>
<td>Stable: Yes</td>
</tr>
<tr>
<td>Oxidising: No</td>
</tr>
<tr>
<td>Hygroscopic: No</td>
</tr>
<tr>
<td>Irritant: No</td>
</tr>
<tr>
<td>Flammable: No</td>
</tr>
<tr>
<td>Handling: See caution, Section 2</td>
</tr>
<tr>
<td>Other (specify):</td>
</tr>
<tr>
<td>Contains dried sheep serum</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Suggested First Aid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation:</td>
</tr>
<tr>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Ingestion:</td>
</tr>
<tr>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Contact with eyes:</td>
</tr>
<tr>
<td>Wash with copious amounts of water.  Seek medical advice</td>
</tr>
<tr>
<td>Contact with skin:</td>
</tr>
<tr>
<td>Wash thoroughly with water.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Action on Spillage and Method of Disposal</th>
</tr>
</thead>
<tbody>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>

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.

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

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

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG, T +44 (0) 1707 641000, nibsc.org

Confidence in Biological Medicines
Medicines & Healthcare products
Regulatory Agency

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16. INFORMATION FOR CUSTOMS USE ONLY

<table>
<thead>
<tr>
<th>Country of origin for customs purposes*:</th>
<th>United Kingdom</th>
</tr>
</thead>
<tbody>
<tr>
<td>* 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.</td>
<td></td>
</tr>
<tr>
<td>Net weight:</td>
<td>0.01g</td>
</tr>
<tr>
<td>Toxicity Statement:</td>
<td>Non-toxic</td>
</tr>
<tr>
<td>Veterinary certificate or other statement if applicable:</td>
<td>No</td>
</tr>
</tbody>
</table>

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_bioolefstandardsrev2004.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.
WHO International Laboratory for Biological Standards

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Telefax:  +45 32 68 31 50 (Laboratory direct)
E-mail (Internet): GAHANSEN@STANDARD.SSL.DK

THE INTERNATIONAL REFERENCE REAGENTS

of

ANTI-TICK-BORNE ENCEPHALITIS SERUM (LOUFING ILL( MOREDUN) VIRUS) AND
ANTI-TICK-BORNE ENCEPHALITIS SERUM (RUSSIAN SPRING-SUMMER
ENCEPHALITIS (SOPHYN AND ABSETTAROV) VIRUS)
(1st international reference reagents)

1. THE REFERENCE REAGENTS

The reference reagents were established in 1964.

The Russian Spring-Summer encephalitis serum was produced by the Institute of
Experimental Medicine, Leningrad by immunization of sheep with two virus
strains, the Sophyn and the Absettarov strains of tick-borne encephalitis
virus. The serum is freeze-dried with 2 ml serum per ampoule. 1 ml reconsti-
tuted serum was found to neutralize $10^{-12}$ virus in experiments with intra-
venous injection of white mice. The serum is not useful in complement
fixation tests.

The Louping ill encephalitis serum is probably prepared in Copenhagen but it
has not been possible to find any information about it.

2. 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 prophylax-
is, therapy, or diagnosis of disease, where this cannot be expressed in terms
of physical or chemical quantities. The International Units are units of
quantities of "effective constituent".

The standard is the material as it exists in the ampoules, the "material" thus
includes the effective constituents together with all the other constituents
that may be present (moisture, carrier, buffer, salt etc., according to the
form in which the standard is available).

International biological reference materials are intended for use in the
calibration of the contents of "effective constituent" in national or working
standard preparations and for the expression of these contents in the
respective International Units. For the routine use in the laboratory the
national or working standards should be used in order to save as much as
possible the international reference materials. These are only sent to
individual laboratories in very limited amounts. The preparations are sent
free of charges but sometimes a small charge might be claimed for the air-
freighting.

January 1997

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1. REFERENCES
