WHO International Standard
Anti-Measles Serum, Human and Anti-Poliovirus serum Types 1, 2 and 3
NIBSC code: 66/202
Instructions for use
(Version 3.0, Dated 01/04/2008)

1. INTENDED USE
The 2nd International Standard for anti-measles serum was established by the Expert Committee on Biological Standardisation, World Health Organisation in 1990. The same material was established in 1991 as the 2nd International Standard for anti-poliovirus 1, 2 and 3. The material consists of ampoules containing equal quantities of the residue after freeze-drying of approximately 1ml of pooled human serum.

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. The material 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
a) Anti-Measles activity. The reconstituted material will contain 5 IU anti-measles activity.
b) Anti-poliovirus activity. The reconstituted material will contain:
   - 25 IU of antipoliovirus serum (type 1) human.
   - 50 IU of antipoliovirus serum (type 2) human.
   - 5 IU of antipoliovirus serum (type-3) human.

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

5. STORAGE
Unopened ampoules should be stored 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
Tap the ampoule gently to collect the material at the bottom (labelled) end. Ensure ampoule is scored all round at the narrow part of the neck, with a diamond or tungsten carbide tipped glass knife file or other suitable implement before attempting to open. Place the ampoule in the ampoule opener, positioning the score at position ‘A’: shown in the diagram below. Surround the ampoule with cloth or layers of tissue paper. Grip the ampoule and holder in the hand and squeeze at point ‘B’. The ampoule will snap open. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.

Side view of ampoule opening device containing an ampoule positioned ready to open. ‘A’ is the score mark and ‘B’ the point of applied pressure.

7. USE OF MATERIAL
No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution.

Reconstitute the total contents of the ampoule in distilled water or a suitable buffer to a known volume.

PREPARATION OF THE STANDARD

The bulk material consisted of a pool of human sera prepared in 1966 and freeze-dried in glass ampoules. The mean filling weight was 1.018g ± 0.4% and the mean residual moisture content was 0.28%. No bacterial contamination was detected in the pool and the freeze-dried material was also negative for HBsAg and HIV antibodies. Half this material was allocated for an anti-polio antibody preparation and half for an anti-measles antibody preparation.

The 2nd International Standard for Anti-Measles serum (66/202) was quantified in a collaborative study involving four laboratories (BS/90/1636). The material was compared with two other freeze-dried anti-Measles sera, namely the International Reference Preparation containing 10IU/ampoule and the British Standard (65/140) containing 5 IU/ampoule. In addition, one laboratory also tested the Danish Standard (6539). Tests were used haemaglutination inhibition, plaque reduction neutralisation and ELISA. Samples of 66/202 which had been held at 45°C for six months were also tested and showed no significant loss of potency.

The results of the study were published in Biologicals (1991) 19, 237-241. Initial communication from the Expert Committee led us to describe 66/202 as the 1st International Standard for anti-measles serum and this was the title of the paper. However, it was later decided that this may cause confusion with the 1st International Reference Preparation, therefore 66/202 was established as the 2nd International Standard.

The 2nd International Standard for Anti-poliovirus serum (66/202) was quantified in a collaborative study which involved nine laboratories (BS/91/1660). The material was compared with four other freeze-dried sera, namely the three International Standard for antipoliovirus sera 1, 2 and 3 and an additional pooled human serum coded 66/161. Neutralising antibody tests were used by all laboratories. Samples of 66/202 which had been held at elevated temperatures for up to 25 months were also tested. The material was very stable with a predicted loss of activity of less than 0.01% per year when stored at –20°C for all three serotypes. The results of this study were published in Biologicals (1992), 20, 203-211.

REPORTING RESULTS OF ASSAYS FOR POLIOVIRUS NEUTRALISING ANTIBODIES IN INTERNATIONAL UNITS

The guidelines for WHO/EPI Collaborative Studies on Poliomyelitis include a Standard Procedure for Measuring Immunity to Poliovirus using the WHO International Standard for anti-poliovirus neutralising antibodies in international units. The guidelines for WHO/EPI Collaborative Studies on Poliomyelitis include a Standard Procedure for Measuring Immunity to Poliovirus using the WHO International Standard for anti-poliovirus neutralising antibodies in international units.

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In-house serum selected for possible reference purposes and the International Standard Poliovirus Antiserum are titrated in parallel on at least 6 separate occasions using 8 replicates per serum dilution.

The geometric mean titre (GMT) of the in-house reference serum is divided by the GMT of the International Standard Antiserum. This result is multiplied by the assigned potency of the International Standard antiserum, thus expressing the titre of the in-house reference in International Units.

EXAMPLE:

GMT of the in-house reference serum = 320
GMT of the International Standard Antiserum = 640
Assigned potency of the International Standard antiserum = 20

Therefore,
Potency of the in-house reference serum = 320/640 x 320 = 10
International Units of polio neutralising antibody.

Expressing results in International Units

The in-house reference should be tested in each assay using 8 replicates per serum dilution. For the assay to be valid, the titre should be within one two fold dilution step of the established GMT of the in-house reference serum.

The titre of the test serum is divided by the established GMT for the in-house reference serum and multiplied by the potency value in IU of the in-house reference serum, thus giving the potency of the test serum in IU. Conversion tables to facilitate calculations can be constructed.

EXAMPLE

<table>
<thead>
<tr>
<th>Virus type</th>
<th>GMT</th>
<th>Acceptable range</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>181</td>
<td>90-362</td>
</tr>
<tr>
<td>2</td>
<td>128</td>
<td>64-256</td>
</tr>
<tr>
<td>3</td>
<td>32</td>
<td>16-64</td>
</tr>
</tbody>
</table>

Potency of the in-house reference serum established by calibration

10.9 IU of type 1 neutralizing antibody
17.2 IU of type 2 neutralizing antibody
2.5 IU of type 3 neutralizing antibody

Potency of a test serum with titres to P1=8, P2=8, P3=8

8. STABILITY
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.

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label. For information specific to a particular biological standard, contact the Technical Information Officer or, where known, the appropriate NIBSC scientist.

In addition, once reconstituted, diluted or aliquoted, users should determine the stability of the material according to their own method of preparation, storage and use.

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

Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES
Not applicable

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.

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**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrosive</td>
<td>No</td>
</tr>
<tr>
<td>Freeze-dried powder</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxidising</td>
<td>No</td>
</tr>
<tr>
<td>Irritant</td>
<td>No</td>
</tr>
<tr>
<td>Hygroscopic</td>
<td>No</td>
</tr>
<tr>
<td>Handling</td>
<td>See caution, Section 2</td>
</tr>
<tr>
<td>Contains material of human origin</td>
<td>No</td>
</tr>
</tbody>
</table>

**Toxicological properties**

<table>
<thead>
<tr>
<th>Effect</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects of inhalation</td>
<td>Not established, avoid inhalation</td>
</tr>
<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>Condition</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Ingestion</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Contact with eyes</td>
<td>Wash with copious amounts of water. Seek medical advice</td>
</tr>
<tr>
<td>Contact with skin</td>
<td>Wash thoroughly with water</td>
</tr>
</tbody>
</table>

**NIBSC**

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

World Health Organization
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: 0.1g |
| 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_bi orefstandardsrev2004.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.