WHO International Standard
1st International Standard for Human Anti-pneumococcal capsule
Reference Serum
NIBSC code: 007sp
Instructions for use
(Version 2.1, Dated 30/06/2014)

1. INTENDED USE
007sp is for use in the enzyme-linked immunosorbent assay protocol for quantification of human IgG antibodies specific for Streptococcus pneumoniae capsular polysaccharides (Pn PS ELISA). 007sp is a pooled serum from 287 healthy volunteers following vaccination with 23 valent pneumococcal polysaccharide vaccine (Pneumovax II®). In order to estimate the concentration of antibodies 007sp antibody concentrations were defined through bridging to the previously established standard 89SF (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 candidate standard was calibrated in an International Collaborative Study involving 5 laboratories (2). These values were derived following double adsorption of 007sp with cell wall polysaccharide (CPS) and polysaccharide 22F and thus in future, when used as a standard, both standard and unknown sera should be double adsorbed (Lot 89SF values were derived following single adsorption and thus the standard and unknown sera are dealt with differently in the current ELISA protocol), flowing bridging to the standard 89SF antibody concentrations in µg/ml were established (see table).

4. CONTENTS
Country of origin of biological material: USA.
007sp consists of 6ml of freeze-dried human serum. Using FDA licensed methods and in accordance with the requirements of directive 98/79, showed sera to be free from Hepatitis B and C virus, syphilis and HIV.

5. STORAGE
Lyophilised serum should remain stable at room temperature but as a precautionary measure for prolonged storage ampoules should be kept in a cold (-20°C) and dark environment. Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING
Vials have a ‘flip-up’ circular cap. Either on the cap or the collar of the vial, there is an indication of the point at which to lever off the cap. This exposes an area of the stopper through which reconstitution and withdrawal of the preparation can be made using a hypodermic needle and syringe. If use of a pipette is preferred, then fully remove the metal collar using, for example, forceps, taking care to avoid cuts by wearing appropriate gloves. Remove the stopper for access. Care should be taken to prevent loss of the contents.

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

The lyophilized serum as received should be suspended in 6 ml of sterile water. Aliquots sufficient for one assay should be prepared and stored at -20°C or colder (not in a freezer with an automatic defrost cycle). Thawed aliquots can be kept up to two week at 4°C.

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.

Dried serum standards are expected to undergo negligible loss of potency during long term storage at the intended storage temperature (3). Once reconstituted, users should determine the stability of the material according to their own method of preparation, storage and use. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

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

9. REFERENCES

10. ACKNOWLEDGEMENTS
Dr Milan Blake who initiated the 007sp development in 2006. This study (Study Protocol number 06-0093) was sponsored by CBER, USFDA.

11. FURTHER INFORMATION
Further information can be obtained as follows:
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 powder
Stable: Yes Oxidising: No
Hygroscopic: No Irritant: Unknown
Flammable: No Handling: See caution, Section 2
Other (specify): N/A

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*: USA
* 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: Approximately 6.12g
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.

Assigned IgG antibody concentrations (µg/ml) for 007sp

<table>
<thead>
<tr>
<th>Type</th>
<th>IgG ELISA Concentration(µg/ml)</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.50</td>
<td>7.88</td>
<td>9.16</td>
</tr>
<tr>
<td>3</td>
<td>1.45</td>
<td>1.36</td>
<td>1.55</td>
</tr>
<tr>
<td>4</td>
<td>3.33</td>
<td>2.95</td>
<td>3.77</td>
</tr>
<tr>
<td>5</td>
<td>7.51</td>
<td>7.04</td>
<td>8.02</td>
</tr>
<tr>
<td>6A</td>
<td>3.93</td>
<td>3.74</td>
<td>4.14</td>
</tr>
<tr>
<td>6B</td>
<td>9.05</td>
<td>7.59</td>
<td>10.80</td>
</tr>
<tr>
<td>7F</td>
<td>8.30</td>
<td>8.14</td>
<td>8.46</td>
</tr>
<tr>
<td>9V</td>
<td>6.44</td>
<td>6.06</td>
<td>6.84</td>
</tr>
<tr>
<td>14</td>
<td>37.99</td>
<td>34.86</td>
<td>41.39</td>
</tr>
<tr>
<td>18C</td>
<td>7.30</td>
<td>6.80</td>
<td>7.84</td>
</tr>
<tr>
<td>19A</td>
<td>13.87</td>
<td>11.51</td>
<td>16.73</td>
</tr>
<tr>
<td>19F</td>
<td>14.61</td>
<td>12.68</td>
<td>16.82</td>
</tr>
<tr>
<td>23F</td>
<td>5.95</td>
<td>5.21</td>
<td>6.81</td>
</tr>
</tbody>
</table>