1. INTENDED USE
The International Standard for Sex Hormone Binding Globulin (SHBG) consists of a batch of ampoules containing freeze-dried serum, obtained from a pool of normal healthy female volunteers. The preparation has been evaluated in an international collaborative study and shown to possess sex hormone binding globulin activity. At its 49th meeting in 1998, the Expert Committee on Biological Standardisation of the World Health Organisation established the preparation coded 95/560 as the International Standard for Sex Hormone Binding Globulin.

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. UNTAGE
107 International units (IU) per ampoule by definition.

The results of the collaborative study indicated that, for the purposes of this preparation, 1 International Unit is equivalent to approximately 1 pmol of SHBG. After reconstitution of ampoule contents in 1ml, this corresponds to 107 IU/ml or approximately 107 nmol/L.

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

Each ampoule contains the freeze-dried residue of 1.0ml of human serum.

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
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
For all practical purposes each ampoule contains the same amount of the above materials. Dissolve the total contents in a known amount of suitable buffer solution with carrier protein (free of peptidase), where extensive dilution is required, to minimise loss by surface adsorption. No attempt should be made to weigh out portions of the freeze-dried powder. For economy of use it is recommended that the solution be subdivided into several small containers, which are frozen rapidly to below -40°C and then stored below -40°C in the dark. Repeated freezing and thawing should be avoided.

The material has not been sterilized and contains no bacteriostat. Suitable precautions should be taken in the use and disposal of the ampoule and its contents: see MATERIAL SAFETY SHEET.

8. PREPARATION OF AMPOULES

Serum for the study was obtained from healthy female volunteers at Nottingham City Hospital. Permission of the local Ethical Committee was obtained and all volunteers were shown to be negative for the presence of infectious agents. All volunteers gave their informed consent. One unit of blood was collected from each volunteer and allowed to clot. The resulting serum was removed and aliquots from each subject were pooled. The pool was distributed into 1ml aliquots in glass ampoules coded 95/560, freeze-dried and subjected to secondary desiccation according to WHO procedures. (1)

9. COLLABORATIVE STUDY

9.1 Design of the Study
The material was evaluated in a collaborative study in which 9 laboratories in 3 countries participated. Participants were requested to examine the candidate preparation by SHBG binding assays and immunoassays, to calibrate the candidate preparation in terms of local standards and to assign a unitage and to assess the residual SHBG activity in ampoules of 95/560 that had been subjected to accelerated thermal degradation.

9.2 Results and Conclusions
The candidate standard material in ampoules coded 95/560 exhibited SHBG activity in all assays, with a mean result from all laboratories of 107 pmol per ampoule. Analysis of ampoules subjected to accelerated thermal degradation indicated that the stability of the material is satisfactory.

Based on the results of the Collaborative Study, and with the agreement of participants in the study, the WHO formally established the preparation coded 95/560 as the international standard for SHBG with a defined content of 107 International Units per ampoule. WHO also noted that for this preparation the mean of all assay determinations in terms of local standards was 107 pmol per ampoule and, therefore, that for the International Standard, 1 International Unit may be considered approximately equal to 1 pmol of SHBG.

10. 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 standards@nibsc.ac.uk. 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.

11. REFERENCES
12. ACKNOWLEDGEMENTS
Acknowledgements are due to Dr Colin Selby of the UK NEQAS scheme for his collaboration and the support of NEQAS in this project.

13. FURTHER INFORMATION
Further information can be obtained as follows:
This material: enquiries@nibsc.org
WHO Biological Standards: http://www.who.int/biologicals/en/
Derivation of International Units: http://www.nibsc.org/standardisation/international_standards.aspx
NIBSC Terms & Conditions: http://www.nibsc.org/terms_and_conditions.aspx

14. 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

15. 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.

16. 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>
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<tr>
<td>Physical appearance: Solid</td>
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<tr>
<td>Corrosive: No</td>
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<tr>
<td>Stable: Yes</td>
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<tr>
<td>Oxidising: No</td>
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<td>Hygroscopic: Yes</td>
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<td>Irritant: No</td>
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<td>Hymorrhagic: Yes</td>
</tr>
<tr>
<td>No</td>
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<tr>
<td>Fiammable: No</td>
</tr>
<tr>
<td>Handling: See caution, Section 2</td>
</tr>
<tr>
<td>Other (specify): Contains material of human origin</td>
</tr>
</tbody>
</table>

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.

17. 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.

18. 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: 30mg
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_Intel_biol_efstandardsrev2004.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.