Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
2nd International Standard for Sex Hormone Binding Globulin
NIBSC code: 08/266
Instructions for use
(Version 2.0, Dated 28/03/2013)

1. INTENDED USE

The first International Standard (IS) for Sex Hormone Binding Globulin (SHBG) in ampoules coded 95/560 was established in 1998 and has been widely used for the calibration of immunoassays and binding assays for the measurement of human serum SHBG levels. The World Health Organization (WHO) Expert Committee on Biological Standardization (ECBS) has recognized (2008) the need for a replacement International Standard for sex hormone binding globulin (SHBG) for the calibration of assays for the measurement of human serum SHBG levels that are important for the diagnosis of conditions associated with abnormal sex steroid function. The 2nd IS, coded 08/266, was established at the 61st Meeting of the ECBS. This material replaces the 1st IS, which is discontinued.

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 contains 180 INTERNATIONAL UNITS, equivalent to 180 pmol per ampoule.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The 2nd IS for SHBG consists of a batch of ampoules, coded 08/266, containing freeze dried serum obtained from a pool of normal healthy female volunteers.
Each ampoule contains the residue after freeze-drying of 1ml of human serum with 40mM HEPES.

5. STORAGE

Unopened ampoules should be stored at –20ºC
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
For practical purposes each ampoule contains the same quantity of SHBG. The entire content of each ampoule should be completely dissolved in an accurately measured amount of distilled water or appropriate assay diluent. The use of PBS to reconstitute ampoule contents is not recommended. If the contents are to be diluted extensively, the addition of 0.05%-0.1% protein (HSA or BSA) is recommended to minimise adsorption. The material has not been sterilized and the ampoules contain no bacteriostat.

COLLABORATIVE STUDY
The preparation was evaluated in a collaborative study in which eleven laboratories in five countries took part, organised with the following aims:

1) To calibrate, by immunoassay and binding assay, the candidate standard 08/266 relative to the 1st IS for SHBG (95/560)
2) To demonstrate the suitability of the candidate preparation 08/266 to serve as the 2nd International Standard for SHBG by examining its behaviour in immunoassay and binding assay systems
3) To assess the relationships among existing local standards and the proposed IS, 08/266
4) To determine the stability of the preparation 08/266 by comparison with ampoules stored at elevated temperatures as part of an accelerated degradation stability study.

The geometric mean potency calculated from immunoassay estimates from all laboratories was 180 IU per ampoule (n=14; 95% confidence limits 176.15 – 184.14; GCV 3.92%), where, for this preparation, 1 IU is equivalent to 1 pmol SHBG.

One laboratory provided steroid binding assay data, which indicated that there may be non-continuity of steroid binding activitiy between 08/266 and the 1st IS, 95/560, as the preparation 08/266 was shown to bind to dihydrotestosterone derivatives with approximately twice the binding potential compared with the 1st IS, 95/560. Binding assay users are therefore recommended to assess the suitability of this preparation in their own assays prior to use.

The candidate preparation 08/282 is sufficiently stable to serve as an International Standard since no significant loss in bioactivity was found at temperatures usually used for storage of biological samples (+4, +20°C). This suggests that 08/282 is likely to be highly stable under long term storage conditions at -20°C.

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.

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

9. REFERENCES

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of all the participants and Dr Jonathan Middle of the UK NEQAS scheme who kindly collected and tested serum samples used in this project.

11. FURTHER INFORMATION

Further information can be obtained as follows;
This material: enquiries@nibsc.org
WHO Biological Standards:
http://www.who.int/biologicals/en/

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

World Health Organization

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: Yellow powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	Yes	Irritant:	No
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	Contains material of human origin		

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 a virucidal agent. Rinse area with a virucidal agent 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: 12mg
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_biolefstandardsrev2004.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.