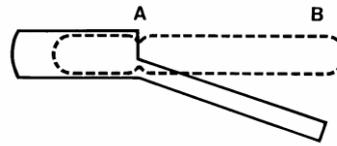




**WHO International Standard
Thyroxine-binding globulin
NIBSC code: 88/638
Instructions for use
(Version 3.0, Dated 09/01/2008)**



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.

1. INTENDED USE

At its 42nd meeting, the Expert Committee on Biological Standardization of the World Health Organization (WHO ECBS 1991) authorized the establishment of the preparation coded 88/638 as the International Standard for Thyroxine-binding globulin (TBG). The Committee noted that for the preparation 88/638, the content of 30IU per ampoule is equivalent to the nominal ampoule content of 30 micrograms thyroxine-binding globulin, as estimated by physicochemical analyses. For further details of this Standard and its collaborative study see Bristow et al (1993).

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.

However, as with all materials of human origin, the preparation cannot be assumed to be free from infectious agents. The container and its contents should be used and discarded according to your own laboratory procedures. Such procedures probably will include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening the container to avoid cuts.

3. UNITAGE

30 INTERNATIONAL UNITS per ampoule, by definition.

The International unit of 88/638 is assigned without uncertainty. Where required, the uncertainty of the ampoule content of 88/638 may be considered to be the coefficient of variation of the fill volume, which was determined to be 0.225%.

4. CONTENTS

Country of origin of biological material: United Kingdom.

Each ampoule contains the freeze-dried residue of 0.5ml of 0.05M sodium phosphate, pH 7.4 which contained:

Lyophilized human thyroxine-binding globulin	30 micrograms
Trehalose	5.0 milligrams

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.

7. USE OF MATERIAL

For practical purposes each ampoule contains the same quantity of TBG. The entire contents of each ampoule should be completely dissolved in an accurately measured amount of buffer solution. No attempt should be made to weigh out portions of the freeze-dried powder. The reconstitution buffer should contain carrier protein.

For economy in use, it is recommended that the solution, without further dilution, is sub-divided into several small containers and stored at -30°C or below. To maintain full activity of such stored aliquots, it is suggested that the solution of ampoule contents, its subdivision and its freezing (using CO₂/ethanol or liquid N₂) is done rapidly.

A dilute solution prepared for use in an assay should be kept cool (eg. 4°C) and should contain not less than 0.1% w/v carrier protein (free of proteolytic enzymes). Repeated freezing and thawing should be avoided. The material has not been sterilized and the ampoules contain no bacteriostat.

8. PREPARATION OF AMPOULES

Bulk material

TBG was purified from human plasma by a combination of affinity, ion-exchange, gel-filtration and hydroxyapatite chromatography, by Professor M. Pepys, of Hammersmith Hospital, London. The final product was characterised by SDS-gel electrophoresis, electrospray mass spectrometry, UV absorption spectroscopy and N-terminal sequencing. It was essentially free of non-TBG contaminants, and exhibited some heterogeneity due to varying degrees of glycosylation

Distribution into ampoules

Ampoules coded 88/638 were prepared according to the procedures used for international biological standards (29th ECBS report, 1978). A weighed portion of TBG was dissolved in a sterile solution of 0.05M sodium phosphate pH 7.4 containing 1% trehalose. The solution was filtered (0.45 microlitres) and distributed in 0.5ml aliquots into ampoules. The ampouled solution was lyophilized, and the ampoules sealed under nitrogen by heat fusion of the glass and stored at -20°C in the dark.

9. COLLABORATIVE STUDY

Six laboratories in four countries participated in a collaborative study to evaluate 88/638 as a standard for TBG assays.

Immunoassays

Assays performed included radioimmunoassays, immunoradiometric assays, immunofluorometric assays, thyroxine-binding immunosorbent assays, radial immuno diffusion and rocket electrophoresis. When compared with local standards, the preparation 88/638 behaved as TBG in all assays. The overall mean of all estimates was 1.19 micrograms TBG (local standard) per micrograms TBG (88/638).

This estimate was consistent with the physicochemical estimate of 30 micrograms TBG per ampoule. Accordingly, the preparation was assigned an ampoule content of 30 IU per ampoule, with the additional information that for the preparation 88/638, 1 IU is equivalent to 1 microgram TBG.

10. STABILITY

Predicted loss of activity -20°C, measured by immunoassay, was generally less than 0.1% per year.

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



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.

11. REFERENCES

WHO Expert Committee on Biological Standardization (1991), 42nd Report. WHO Technical Report Series No. 822, p14.

Bristow, A.F., Gaines-Das, R.E., Battress, N., Gallimore, J.R. Tennent, G.A. and Pepys, M.B. (1993). Clin. Endocrinol., 38, 361-366.

12. ACKNOWLEDGEMENTS

Grateful acknowledgements are due to Professor Mark Pepys for preparing and donating the TBG preparation and to the participants in the study.

13. 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

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

Physical and Chemical properties	
Physical appearance: Freezed powder	dried
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 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: 5mg
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_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.