



**WHO International Standard
Thyroid-Stimulating Hormone, Recombinant, for Bioassay
NIBSC code: 03/192
Instructions for use
(Version 3.0, Dated 07/02/2008)**

1. INTENDED USE

The World Health Organization (WHO) Expert Committee on Biological Standardization (ECBS) recognized the need (2004) for an international standard for bioassay of recombinant human thyroid stimulating hormone (rhTSH) in terms of which the activity of therapeutic products could be expressed. A preparation of CHO-cell derived rhTSH was donated to the WHO and distributed into ampoules (Code No. 03/192) at NIBSC, the content of which was assigned in International Units (IU) by international collaborative study and established as the 1st International Standard for Thyroid-Stimulating Hormone, Human, for Bioassay by the ECBS in October 2006 (WHO/BS/06.2048). This document is available from WHO and describes the characterization of the candidate standard for rhTSH in the international collaborative study in seven laboratories in four countries, and its comparison with current TSH reference preparations. The results of the study indicated that the candidate standard had appropriate biological activity, was sufficiently stable on the basis of a thermally accelerated degradation study, and was thus suitable to serve as an international standard.

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The material is not of human or bovine origin. 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 of 03/192 contains 9.5 IU per ampoule (by definition).

Uncertainty: the assigned unitage is arbitrary and does not carry an uncertainty associated with it. When necessary, the uncertainty may be considered to be the coefficient of variation of the ampoule content, and was determined as $\pm 0.07\%$ (cv)

4. CONTENTS

Country of origin of biological material: United Kingdom.

Each ampoule contains the residue after freeze-drying of 1.0 ml of a solution that contained:

Recombinant TSH nominally	0.87 mg
Sodium phosphate	2.6 mg
Sodium chloride	2.0 mg
Mannitol	30 mg

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. 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 manufacturers 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 thyroid-stimulating hormone. The entire content of each ampoule should be completely dissolved in an accurately measured amount of diluent. No attempt should be made to weigh out portions of the freeze-dried powder. Suitable diluents are PBS, saline and most assay buffers. 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 use of water to reconstitute ampoule contents is not recommended. The material has not been sterilized and the ampoules contain no bacteriostat.

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.

Stability studies at elevated temperatures have shown that the material is suitably stable for shipment at ambient temperature without any effect on the assigned value. Reference Materials should be stored on receipt as indicated on the label. 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. 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

10. 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

11. 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.

based on the report of the international collaborative study which established their suitability for the intended use.

12. 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	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify): none	
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 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: 36mg
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)