



**WHO International Standard
Thyroid Stimulating Hormone, Human, for Immunoassay
NIBSC code: 81/565
Instructions for use
(Version 6.0, Dated 08/04/2015)**

1. INTENDED USE

This consists of a batch of ampoules, coded 81/565, containing thyroid-stimulating hormone derived from the same pituitary extract as the 2nd IRP for TSH 80/558, stocks of which are now exhausted. The preparation was examined by international collaborative study and established as the 3rd International Standard for Thyroid-Stimulating Hormone, Human, for Immunoassay by the Expert Committee on Biological Standardization of the World Health Organization in November 2003.

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 probably will 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 81/565 contains 11.5 mIU per ampoule (by definition). Uncertainty: the assigned unitage is arbitrary and does not carry an uncertainty associated with its calibration. The uncertainty may therefore be considered to be the variance of the ampoule content, and was experimentally measured as $\pm 0.38\%$ (cv)

4. CONTENTS

Each ampoule contains the residue after freeze-drying of 0.5 ml of a solution that contained:

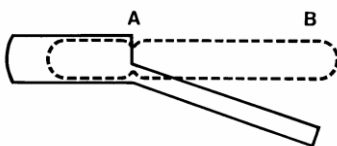
Purified human pituitary TSH extract	nominally 2 µg TSH
Peptidase-free human serum albumin	1mg
Lactose	5 mg

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

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.



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.

7. USE OF MATERIAL

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 buffer solution. No attempt should be made to weigh out portions of the freeze-dried powder. The use of water to reconstitute ampoule contents is not recommended. The material has not been sterilized and the ampoules contain no bacteriostat.

8. PREPARATION OF AMPOULES

A quantity of highly purified extract was prepared and donated by Dr AF Parlow (Harbor-UCLA Medical Centre, Torrance, CA, USA; parlow@humc.edu) through the National Hormone and Pituitary Program (NHPP) of the USA. Ampouling, lyophilisation and sealing of the pituitary TSH preparation 81/565 were carried out according to procedures laid down by WHO for International Biological Standards (WHO 1978) and have been described previously (Gaines Das & Bristow 1985). Briefly, purified pituitary TSH extract was dissolved in a sterile solution containing 0.2% (w/v) peptidase-free human serum albumin and 1% (w/v) lactose. The solution was passed through a membrane filter (0.45µm) and distributed in 0.5 ml aliquots into ampoules. Check weights were carried out during the filling procedure as an estimate of variance in ampoule content and the residual moisture content of the lyophilised material was also determined. These were 0.502 g (CV 0.38%) and 0.08% respectively.

9. COLLABORATIVE STUDY

The candidate pituitary TSH preparation 81/565, along with other pituitary TSH preparations, was evaluated in an international collaborative study in which nine laboratories in six countries took part. Assays contributed were all immunoassays except for a single in vitro assay based on cAMP release from bovine thyroid membranes. The study was designed to:

- compare by immunoassay the ampouled preparations of TSH with local standards presently in use,
- confirm the calibration of the candidate preparation of TSH for use as a potential International Standard,
- confirm the activity of the candidate preparation relative to the original study preparations,
- assess the stability of the candidate preparation using thermally accelerated degradation samples,
- compare rDNA TSH and pituitary TSH in a variety of immunoassay systems.

9.1 Activity of ampoule contents

The main function of preparation 81/565 is to serve as a primary reference reagent against which secondary standards for immunoassay of TSH are calibrated. On the basis of the immunoassay results from the collaborative study, 81/565 was established by the ECBS of WHO as the 3rd International Standard for TSH, Human, for Immunoassay with a defined content of 11.5 mIU per ampoule. This preparation replaces the 2nd IRP for TSH, 80/558. All attempts have been made to ensure the continuity of the unit as evidenced by the results from the majority of assay systems in the study. However this cannot be guaranteed for all assay systems and recalibration may be necessary.

9.2 Stability

Combining the results of accelerated degradation studies by all assay methods a predicted loss of 0.04% per year at -20°C was calculated, indicating that the ampouled preparation 81/565 is sufficiently stable to serve as reference reagent.

10. STABILITY

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. For information specific to a particular biological standard contact, where known, the appropriate NIBSC scientist.

In addition, once reconstituted, diluted or aliquoted, users should determine the stability of the material according to their own method of preparation,

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

11. REFERENCES

1. WHO Tech Rep Ser No 626, 1978
2. Gaines Das RE. & Bristow AF. (1985). The Second International Reference Preparation of Thyroid-Stimulating Hormone, Human, for Immunoassay: calibration by bioassay and immunoassay in an international collaborative study. J. Endocr. 104, 367-379.

12. 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

13. 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

14. 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.

15. 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: Frozen powder	Corrosive: No dried
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	
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.	

16. 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.

17. 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: 6mg
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.