



**WHO International Standard  
Follicle Stimulating Hormone, Pituitary  
NIBSC code: 83/575  
Instructions for use  
(Version 4.0, Dated 06/04/2013)**

## 1. INTENDED USE

This consists of a batch of ampoules coded 83/575 which was established as the International Standard for Follicle Stimulating Hormone, Pituitary at the 37<sup>th</sup> Meeting of the WHO Expert Committee on Biological Standardization (WHO ECBS) in 1986 (WHO ECBS, 1987). For further details of this Standard and of its collaborative study see Storing and Gaines Das (1989).

## 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

Each ampoule contains 80 International Units (by definition).

Uncertainty: the International Unit of 83/575 is assigned without uncertainty. Where required, the uncertainty of the ampoule content of 83/575 may be considered to be the co-efficient of variation of the fill volume, which was determined to be 0.39%.

## 4. CONTENTS

Country of origin of biological material: United Kingdom.  
Each ampoule contains the residue, after freeze-drying, of 0.5ml of a solution which contained:-

FSH extract	approx	4.17µg
Mannitol	approx	5mg
Human plasma albumin	approx	1mg
Sodium chloride	approx	0.6 mg

Nitrogen gas at slightly less than atmospheric pressure

## 5. STORAGE

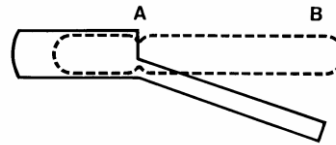
Unopened ampoules should be stored at -20°C.

**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 the above materials. Dissolve all the contents in a known amount of buffer solution. No attempt should be made to weigh portions of the freeze-dried powder.

For economy of use the solution can be kept for several months if an anti-bacterial preservative is added and the solution is subdivided into several small containers, which are frozen rapidly to below -70°C and then stored below -30°C in the dark; repeated freezing and thawing should be avoided. If extensive dilutions are prepared, a carrier protein (0.1% w/v) should be added, which is free of peptidase.

The material has not been sterilized and contains no bacteriostat.

## 8. PREPARATION OF AMPOULES

Highly purified FSH was isolated from human pituitary glands and characterised by Professor W.R Butt and Dr S.S Lynch and their colleagues in Birmingham and generously donated to WHO. This preparation had a biological potency by *in vivo* bioassay (Steelman and Pohley, 1953) of greater than 15,000 IU/mg, at least as high as that found for other highly purified preparations (Storing *et al.* 1981). The preparation was shown to be free from significant contamination with LH and TSH.

This FSH preparation was diluted in a solution containing 0.2% (w/v) heat-treated re-purified human plasma albumin (batch AKII, Lister Institute, Elstree), 1 (w/v) mannitol and 15.4mM sodium chloride. The solution was distributed into ampoules coded 83/575 as approximately 0.5ml aliquots. The ampoule contents were freeze-dried, secondarily desiccated and sealed under nitrogen (Campbell, 1974; WHO ECBS, 1978). The batch consisted of 3872 ampoules. The mean weight of solution in each of 80 weighed ampoules was 0.503g with a range as % of mean of 0.78%.

## 9. COLLABORATIVE STUDY AND THE ASSIGNMENT OF UNITAGE

The collaborative study was carried out by 27 laboratories in 13 countries, in which the preparation of FSH in ampoules coded 83/575 was assayed against the second International Reference Preparation of FSH and LH, Pituitary, for Bioassay (in ampoules coded 78/549).

Estimates of the biological potency of this material by the *in vivo* assay method (based on the increase of ovarian weight in hCG treated immature rats) gave a mean value of about 80 IU/ampoule; estimates with *in vitro* bioassay and hormone receptor-binding assay systems gave heterogeneous values which varied between 5 and 31 IU/ampoule with a mean of about 16 IU/ampoule. In accordance with its policy (WHO ECBS 1982), the WHO Expert Committee on Biological Standardisation agreed that the potency assigned to the new standard should be made on the basis of the results of the *in vivo* bioassays (WHO, ECBS 1987). Such assays reflect the ability of FSH glycoprotein isohormones and their metabolites to exert their full natural *in-situ* biological actions.

The committee recognized, however, that the introduction of the new International Standard, with a defined potency of 80 IU/ampoule will



necessitate the recalibration of many immunoassay kits. Because immunoassays of FSH are widely used clinically, and critical decisions depend upon their results, the Committee agreed that manufacturers should state clearly with which standard their kit has been calibrated and that calibration against the new International Standard should be adopted as rapidly as possible.

#### 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.

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.

#### 11. REFERENCES

Campbell, P.J.,(1974). J. Biol. Standardization. 2:259-267  
 Steelman, S.L. & Pohley, R.M. (1953). Endocrinology, 53:604-616  
 Storing, P.L. & Gaines-Das, R.E. (1989). J. Endocrinol. 123:275-293  
 Storing, P.L., Zaidi, A.A., Mistry, Y.G., Froya, B., Stenning, B.E., Diczfalusy, E. (1981). J. Endocrinol. 91:353-362  
 WHO Expert Committee on Biological Standardization (1978). WHO Tech Rep Ser No 626  
 WHO Expert Committee on Biological Standardization (1982). WHO Tech Rep Ser No 673  
 WHO Expert Committee on Biological Standardization (1987). WHO Tech Rep Ser No 760

#### 12. ACKNOWLEDGEMENTS

Grateful acknowledgements are due to: the participants in the collaborative study; Professor W.R Butt and Dr S.S Lynch and their colleagues for isolating and characterising the FSH from which the standard was prepared; and to Dr P. J Campbell for ampouling.

#### 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](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](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 dried 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 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](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

<b>Country of origin for customs purposes*:</b> 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.
<b>Net weight:</b> 7mg
<b>Toxicity Statement:</b> Non-toxic
<b>Veterinary certificate or other statement</b> if applicable.
<b>Attached:</b> 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](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) based on the report of the international collaborative study which established their suitability for the intended use.