



**WHO International Standard  
2nd International Standard for Follicle-Stimulating Hormone,  
human, recombinant, for bioassay  
NIBSC code: 08/282  
Instructions for use  
(Version 3.0, Dated 28/03/2013)**

### 1. INTENDED USE

The first International Standard (IS) for recombinant human FSH (rhFSH) in ampoules coded 92/642 was established in 1995 and has been widely used for the calibration of preparations of recombinant DNA-derived human FSH by bioassay. The World Health Organization (WHO) Expert Committee on Biological Standardization (ECBS) has recognized (2009) the need for a replacement International Standard for Follicle-stimulating hormone (FSH) for the assignment of potency to therapeutic preparations of recombinant human FSH used in the treatment of infertility. The 2nd IS, coded 08/282 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 126 INTERNATIONAL UNITS

### 4. CONTENTS

Country of origin of biological material: United Kingdom.  
Each ampoule contains the residue after freeze-drying of 1ml of a solution that contained:

Recombinant DNA-derived FSH	approximately 10µg.
Human plasma albumin	0.2%w/v
Mannitol	1% w/v
Sodium chloride	15.4mM

### 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 rhFSH. The entire content of each ampoule should be completely dissolved in an accurately measured amount of buffer solution. The use of

water to reconstitute ampoule contents is not recommended. The material has not been sterilized and the ampoules contain no bacteriostat.

### COLLABORATIVE STUDY

The preparation was evaluated in a collaborative study in which fourteen laboratories in ten countries took part, organised with the following aims:

- 1) To calibrate the candidate standard 08/282 relative to the 1st IS for rhFSH (92/642) by in vivo and in vitro bioassay.
- 2) To assess the suitability of the candidate preparation 08/282 to serve as the 2nd International Standard for the calibration of therapeutic FSH products by bioassay.
- 3) To determine the stability of the preparation 08/282 by comparison with ampoules stored at elevated temperatures as part of an accelerated degradation stability study.

The geometric mean potency calculated from all laboratories using organ weight as assay response was 126.0 IU per ampoule (n=14; 95% confidence limits 118.7 – 133.7; GCV 10.8%). For in vivo bioassays only, the mean was 126.6 IU per ampoule (n=12; 95% confidence limits 118.8 - 134.9; GCV 10.5%). The geometric mean potencies calculated using alternative assay responses were in agreement with these values.

The candidate preparation 08/282 is sufficiently stable to serve as an International Standard since no significant loss in bioactivity was found at any of the elevated temperatures. 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 Merck Serono, the pharmaceutical division of Merck KGaA, Darmstadt (Germany) for the kind donation of the rhFSH.

### 11. FURTHER INFORMATION

Further information can be obtained as follows;  
This material: [enquiries@nibsc.org](mailto: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)

## 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: White powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Can react with oxidising materials. Avoid contact with acids and alkalis.
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.	

## 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](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

<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> 12mg
<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\\_biol\\_efstandardsrev2004.pdf](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.