Non WHO Reference Material
Follicle Stimulating Hormone
Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified
Luteinizing Hormone, Human, Pituitary
NIBSC code: 94/632
Instructions for use
-Version 5.0, Dated 23/09/2010

This material is not for in vitro diagnostic use.

1. INTENDED USE

Stocks of the 2nd International Reference Preparation for Follicle Stimulating Hormone/Luteinizing Hormone (ICSH), Human, Pituitary for Bioassay, (Code number 78/549) (1 & 2) are exhausted. Because this preparation was widely used for calibration of commercial diagnostic kits for FSH determination and because the International Standard for Follicle Stimulating Hormone, Pituitary (Code 83/575) appeared to be unacceptable for this purpose a further batch of ampoules (Coded 94/632) was filled with material contained in master ampoules (Code 69/133) used for preparation of the 1st and 2nd IRP (Coded 69/104 and 78/549 respectively). The preparation in ampoules coded 94/632 was made available as an interim reference preparation to replace the 2nd IRP pending the completion of an International Collaborative Study to evaluate candidate standards for rDNA-derived human follicle stimulating hormone. This study has now been completed and although ampoules of 94/632 are still available users of this material should pay particular attention to section 9 of this memorandum.

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

For use in immunoassays, users of this material are recommended to assume a unitage of 20 IU FSH per ampoule.

Uncertainty: the International Unit of 94/632 is assigned without opening ampoules or vials, to avoid cuts. Procedure potentially hazardous to health. It should be used and discarded all materials of biological origin, this preparation should be regarded as

4. CONTENTS

Country of origin of biological material: United Kingdom.

Each ampoule contains the residue, after freeze drying and secondary desiccation, of 1.0 ml of a solution which contained:

- Extract of human pituitaries 1.0 mg
- Lactose 2.5 mg
- Dry nitrogen 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

DIN ampoules have an ‘easy-open’ coloured stress point, where the narrow ampoule stem joins the wider ampoule body.

Tap the ampoule gently to collect the material at the bottom (labeled) end. Ensure that the disposable ampoule safety breaker provided is pushed down on the stem of the ampoule and against the shoulder of the ampoule body. Hold the body of the ampoule in one hand and the disposable ampoule breaker covering the ampoule stem between the thumb and first finger of the other hand. Apply a bending force to open the ampoule at the coloured stress point, primarily using the hand holding the plastic collar.

Care should be taken to avoid cuts and projectile glass fragments that might enter the eyes, for example, by the use of suitable gloves and an eye shield. Take care that no material is lost from the ampoule and no glass falls into the ampoule. Within the ampoule is dry nitrogen gas at slightly less than atmospheric pressure. A new disposable ampoule breaker is provided with each DIN ampoule.

7. USE OF MATERIAL

For practical purposes each ampoule contains the same amount of the same 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 then stored below 70°C.

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 sterilised and contains no bacteriostat.

8. PREPARATION OF AMPOULES AND ACTIVITY OF CONTENTS

A batch of 1162 ampoules was prepared using the content of three master ampoules (Code 69/133) using procedures as similar as possible to those used for preparing the 1st and 2nd International Reference Preparation.

9. INTERNATIONAL STANDARD FOR FSH, HUMAN, RECOMBINANT

The Second International Reference Preparation for FSH and LH, human pituitary (in ampoules coded 78/549) has been used as a universal calibrator for diagnostic immunoassays. However, supplies of this preparation are now exhausted and NIBSC has therefore recently issued an interim reference preparation which was derived from the same master ampoules as the IRP described in this memorandum. Supplies of this material are also limited and when stocks become exhausted it will not be possible to replace it with a similar material. Moreover the material from which both the First and Second IRPs and the interim reference preparation were derived is very impure and therefore poorly defined in terms of the gonadotrophin content and therefore does not represent an ideal standard for calibration of different immunoassay systems. The relative impurity has been a contributing factor to the difficulty experienced in calibrating candidate standards for highly purified FSH either by immunoassay or bioassay whilst maintaining a continuity of unitage.

Following completion of the International Collaborative Study to evaluate candidate International Standards for recombinant DNA derived FSH, the First International Standard for FSH, human, recombinant for bioassay, 92/642, was established by ECBS of WHO. However, at that time no decision was made regarding the establishment of any preparation to serve as an International Standard for Immunoassay. The issues surrounding this particular problem were discussed in some detail at a workshop held at NIBSC in March 1996 (5) and the materials included in the collaborative study were included in two distributions through the UK NEQAS scheme (6).
Having reviewed the available data from these studies and considering the availability of current preparations used for calibration of diagnostic immunoassays a proposal was made for establishing the ampouled reference preparation to exhibit the potency as described at establishment.

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.

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.

10. STABILITY

In the absence of stability data, users should assume the interim reference preparation to exhibit the potency as described at establishment.

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

5. Jeffcoat S.L. Clinical Endocrinology (1997) 46 527 529

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/standardsisation/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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical appearance: Freeze dried powder</td>
</tr>
<tr>
<td>Stable: Yes</td>
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<tr>
<td>Hygroscopic: Yes</td>
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<tr>
<td>Flammable: No</td>
</tr>
<tr>
<td>Other (specify): Contains material of human origin</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th><strong>Country of origin for customs purposes</strong>: United Kingdom</th>
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<tbody>
<tr>
<td>* 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.</td>
</tr>
<tr>
<td><strong>Net weight</strong>: 4mg</td>
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<tr>
<td><strong>Toxicity Statement</strong>: Non-toxic</td>
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<tr>
<td><strong>Veterinary certificate or other statement</strong> if applicable, Attached: No</td>
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