Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Prolactin, Human.
NIBSC code: 84/500
Instructions for use
(Version 4.0, Dated 06/04/2013)

1. INTENDED USE

The material consists of a batch of ampoules (coded 84/500) which was established as the 3rd International Standard at the 39th Meeting of the Expert Committee on Biological Standardization of WHO, Geneva[1,2].

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 of the International Standard contains 53 MILLI INTERNATIONAL UNITS (by definition).

4. CONTENTS

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

Human prolactin	approx 2.5 µg
Human albumin	" 1 mg
Lactose	" 5 mg
Ammonium formate	" 0.63 mg

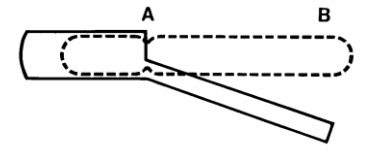
Pure dry nitrogen at slightly less than atmospheric pressure.

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

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 all practical purposes, each ampoule contains the same quantity of the substances listed above. Dissolve the total contents of the ampoule in a known volume of a suitable solvent with carrier protein where extensive dilution is required.
No attempt should be made to weigh out any portion of the freeze-dried material.
For economy of use, it is recommended that the solution be sub-divided into several small containers and stored at -40°C, or below.
The ampoules do not contain bacteriostat and solutions of them should not be assumed to be sterile.

8. PREPARATION OF AMPOULES

A quantity of highly purified extract was donated by Dr S. S Lynch and Professor W R Butt (Birmingham & Midland Hospital for Women, Birmingham, UK). The material consisted of a single batch (H-Prol SFK2) provided as a frozen solution in 0.01M ammonium acetate. The bulk solution (35.46ml; 10mg protein) was dissolved in 4.0L of a solution, pH 6.8, containing 0.01M ammonium formate, 0.1% human albumin and 0.5% lactose and sterilized by membrane filtration. The solution was filtered through a Millex HA (Millipore, Bedford, MA, USA) membrane, mean pore diameter 0.4 micrometres. Some 4000 ampoules were filled with 1.0g of the solution maintained at 4°C. The ampouled solution was then pre-frozen to -35°C, freeze-dried and further desiccated *in vacuo*. The ampoules were then filled with pure dry nitrogen and sealed by glass fusion (Annex 4, 29th ECBS Report, 1978)[3]. The mean weight of solution filled in 80 weighed ampoules was 1.002gm, range ± 0.2% of the mean.

9. CONTAMINANTS

Radioimmunoassay indicated contamination with human growth hormone of about 0.5% by weight (some of this may represent cross-reaction with hPRL).

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

Ampoules of 84/500 which had been stored for 84 and 692 days at elevated temperatures were examined in a few assay systems. Comparison of these samples with the samples stored continuously at -20°C, suggests that in general no immunologically detectable degradation has occurred; at -20°C the detectable loss is likely to be less than 0.1% per year, although this may be dependent on the assay system used.

11. REFERENCES

1. 39th Report, WHO Expert Committee on Biological Standardization (1989) WHO Tech Rep Ser No. 786.
2. Schulster D, Gaines Das R E & Jeffcoate S L (1989). International standards for human prolactin: calibration by international collaborative study. J Endocrinol 121:157-166.
3. Annex 4, 29th Report WHO Expert Committee on Biological Standardization (1978). WHO Tech Rep Ser No. 626.

12. FURTHER INFORMATION

Further information can be obtained as follows;
This material: enquiries@nibsc.org

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

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: Freeze 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.	

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: 7mg
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_biolefstandardsrev2004.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.