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 1978.

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 when 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.

WHO International Standard
Prolactin, Human.
Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified
NIBSC code: 84/500
Instructions for use
(Version 4.0, Dated 06/04/2013)

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 Millipore 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). 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

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.
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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical appearance: Freeze dried powder</td>
<td></td>
</tr>
<tr>
<td>Corrosive:</td>
<td>No</td>
</tr>
<tr>
<td>Stable: Yes</td>
<td></td>
</tr>
<tr>
<td>Oxidising:</td>
<td>No</td>
</tr>
<tr>
<td>Hygroscopic: Yes</td>
<td></td>
</tr>
<tr>
<td>Handling: See caution, Section 2</td>
<td></td>
</tr>
<tr>
<td>Flammable: No</td>
<td></td>
</tr>
<tr>
<td>Irritant:</td>
<td>No</td>
</tr>
<tr>
<td>Other (specify):</td>
<td>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

| Country of origin for customs purposes*: United Kingdom |
| Toxicity Statement: Non-toxic |
| Veterinary certificate or other statement if applicable. Attached: No |

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.

Country of origin for customs purposes*: 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.