Non WHO Reference Material
Parathyroid Hormone, Bovine, for Bioassay
NIBSC code: 76/572
Instructions for use
(Version 4.0, Dated 30/11/2007)

This material is not for in vitro diagnostic use.

1. INTENDED USE
Two independently prepared batches of highly purified bovine parathyroid hormones were pooled and used for amputing. One batch was extracted and purified (on Sephadex G100) by Dr J.L.H. O’Riordan, Middlesex Hospital, London, and the other batch was extracted and purified (Ultrogel AcA54) by Dr J.M. Zanelli at NIBSC in collaboration with Dr J.S. Woodhead, Cardiff and Dr J.A. Parsons, MRC, Mill Hill, London. Minor modifications of the classical phenol extraction, trichloroacetic acid precipitation procedure (Aurbach, 1959) were used for each preparation. Both batches were analysed independently by Dr H. Keutmann, Boston, USA. Amino acid analysis and end terminal (Edman degradation) analysis confirmed that each batch consisted of 90-95% pure bovine parathyroid hormone. Each batch had biological activity of approximately 2500 IU/mg in in vivo (chick hypercalcæmia) and in vitro (renal membrane adenylyl cyclase activation) bioassays.

2. CAUTION
This preparation is not for administration to humans or animals in the human food chain.
The material is of bovine origin. The material is certified to be obtained from animals taken from a closed herd in the female line since 1980, in which no animal has been clinically suspected of having BSE & which has not been fed rations containing ruminant derived protein during that period. 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
230 IU/ampoule.

4. CONTENTS
Country of origin of biological material: United Kingdom.
Each ampoule contains the freeze-dried residue of approximately 0.5ml solution of Parathyroid hormone extract approx 100µg Mannitol (AR grade) as carrier 5mg

The amputing was carried out under conditions used for clinical preparations at Armour Pharmaceutical Co., Eastbourne, Sussex.
The hormone and the mannitol was dissolved in 0.001% acetic acid in double glass distilled water and sterilized by membrane filtration. The solution was distributed into sterile needle glass ampoules and freeze-dried. The mean weight of solution in each of 20 weighed ampoules was 0.508g (±0.6%). After they had been freeze-dried, ampoules were filled with nitrogen and sealed by glass fusion. The batch was tested for leaks and then stored at -20°C in the dark.

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
This reagent replaces the MRC Reagent 72/286 and is intended for bioassay of parathyroid hormone.
No attempt should be made to weigh out any portion of the freeze-dried material. For in vivo bioassays, a suitable solvent is 1% sodium acetate, containing 0.1% albumin (free of protease activity) adjusted to pH 4 using glacial acetic acid. It should be noted that Reagent 76/572 does not contain a bacteriostat.

This reagent is not for administration to humans.

8. BIOLOGICAL ACTIVITY OF NIBSC REAGENT 76/572
The potency of the reagent was estimated on the basis of in vivo intravenous and subcutaneous assays, carried out at the National Institute for Medical Research, Mill Hill and the National Institute for Biological Standards and Control, Hampstead, against MRC Reagent 72/286 (calibrated against the 1st International Reference Preparation of Parathyroid Hormone, bovine for Bioassay). The combined estimate of potency was 232 IU/ampoule, 95% confidence limits 87%-114%.

From the data obtained in this study, a potency of 230 IU/ampoule has been assigned to NIBSC Reagent 76/572.

9. 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. For information specific to a particular biological standard contact the appropriate NIBSC scientist.
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.

10. 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/standards/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
11. 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

12. 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.

13. MATERIAL SAFETY SHEET
Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
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<tbody>
<tr>
<td>Physical appearance: Freeze dried powder</td>
<td>Corrosive: No</td>
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<tr>
<td>Stable: Yes</td>
<td>Oxidising: No</td>
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<tr>
<td>Hygroscopic: Yes</td>
<td>Irritant: No</td>
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<tr>
<td>Flammable: No</td>
<td>Handling: See caution, Section 2</td>
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<tr>
<td>Other (specify): Contains material of bovine origin</td>
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<table>
<thead>
<tr>
<th>Toxicological properties</th>
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<tbody>
<tr>
<td>Effects of inhalation: Not established, avoid inhalation</td>
<td></td>
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<tr>
<td>Effects of ingestion: Not established, avoid ingestion</td>
<td></td>
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<tr>
<td>Effects of skin absorption: Not established, avoid contact with skin</td>
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<tr>
<th>Suggested First Aid</th>
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<tbody>
<tr>
<td>Inhalation: Seek medical advice</td>
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<tr>
<td>Ingestion: Seek medical advice</td>
<td></td>
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<tr>
<td>Contact with eyes: Wash with copious amounts of water. Seek medical advice</td>
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<tr>
<td>Contact with skin: Wash thoroughly with water.</td>
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<tr>
<th>Action on Spillage and Method of Disposal</th>
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<tr>
<td>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.</td>
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14. 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.

15. INFORMATION FOR CUSTOMS USE ONLY

| Country of origin for customs purposes*: United Kingdom |
| To be 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: 5mg |
| Toxicity Statement: Non-toxic |
| Veterinary certificate or other statement if applicable. Attached: No |

*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.