DIRECTIONS FOR OPENING

Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature. Non WHO Reference Material

NIBSC Research Standard for Parathyroid Hormone, Human, for Immunoassay
NIBSC code: 75/549
Instructions for use

(Version 4.0, Dated 30/11/2007)

This material is not for in vitro diagnostic use.

1. INTENDED USE

At its 26th meeting, the World Health Organization Expert Committee on Biological Standardization (1975) noted that immunassays of human parathyroid hormone were of value in various clinical situations, and agreed that a need existed for purified human parathyroid hormone to be used as reference material in such assays. The Committee asked the National Institute for Biological Standards and Control, London, in collaboration with interested workers, to obtain material that could serve as an international reference preparation. Owing to the scarcity of such material, the Committee particularly emphasized the desirability of international collaborative efforts to prepare and characterize the preparation. In the ensuing period, a sufficient quantity of highly purified human parathyroid hormone for this purpose was not available. However, a small quantity of partially purified human parathyroid hormone was donated for evaluation by international collaborative study, and has been designated NIBSC Research Standard for human parathyroid hormone for immunassay (Code no. 75/549). Ampoules are estimated to contain approximately 25ng parathyroid hormone and have an assigned potency of 0.025 units.

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 HTV 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 probably will 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. CONTENTS

Human parathyroid hormone approx. 25ng*
Albumin 250μg
Lactose 1.25mg

*Ampoules nominally contain 250ng of a partially purified extract of human parathyroid adenomata, estimated to be approximately 10% pure.

4. STORAGE

Unopened ampoules should be stored at -20°C

5. 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.

6. STABILITY

It is the policy of WHO not to assign an expiry date to these 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. NIBSC follows the policy of WHO with respect to its reference materials. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

7. USE OF AMPOULED MATERIAL

For all practical purposes, each ampoule of the Research Standard contains the same quantity of the above substances. Dissolve the total contents of the ampoule in a known content of a suitable buffer, such as 0.05M sodium barbitone, adjusted to pH 8.6 using concentrated hydrochloric acid and containing at least 0.2% crystalline albumin, free of protease activity (Caygill, 1977), to minimize loss of peptide by surface adsorption. No attempt should be made to weigh out any portion of the freeze-dried material as it cannot be assumed that the parathyroid hormone is distributed homogeneously. Although this ampouled preparation has not been assessed by in vivo bioassay, it has the qualitative biological activities that might be expected in 3 different in vitro systems (including cytochemical bioassay; Chambers et al., 1978) used for the bioassay of the bovine hormone. For economy in use, particularly in immunoassay, aliquots of the stock solution may be snap-frozen and stored at -40°C for several months. The stability of such aliquots should be carefully assessed within the assay system in which they are to be used.

8. BULK MATERIAL

The material used for NIBSC Research Standard for parathyroid hormone, human, was kindly donated by Dr. J.S. Woodhead (University Hospital, Cardiff, Wales) and Dr. M. Peacock (MRC Mineral Metabolism Unit, Leeds, England). Fresh frozen human parathyroid adenomata was collected, pooled, defatted, extracted with phenol and the hormone precipitated with trichloroacetic acid (Aurbach, 1959). Further purification was carried out by gel filtration on Ultrogel AcA54 (LKB Instruments Ltd., Croydon, Surrey).

9. DISTRIBUTION INTO AMPOULES

(Procedure as described in Annex 4, WHO Expert Committee on Biological Standardisation Report, 1978).

In 1975, 630μg of the extract was dissolved in 630ml 0.001M acetic acid in double glass distilled water containing 0.5% lactose and 0.1% albumin, free of peptidase activity and sterilised by membrane filtration. The solution was distributed into approximately 2400 neutral glass ampoules, coded 75/549, and freeze-dried. The mean weight of solution in each of 80 weighed ampoules was 0.254g (range, as percentage of the mean, 0.39%). After secondary desiccation the ampoules were filled with pure dry nitrogen and sealed by glass fusion. After testing for leaks, the batch of ampoules was stored at -20°C in the dark. Samples were negative for the presence of hepatitis B antigen.

10. COLLABORATIVE STUDY

(See Zanelli and Gaines Das, 1980, for the full report).
Seventeen laboratories in 10 countries participated in the international collaborative study of the Research Standard. Other ampouled preparations included in the study were the international Reference Preparation for Parathyroid Hormone, Bovine, for Immunoassay (coded 71/324), samples of human plasma or serum from patients with primary or secondary hyperparathyroidism and a Quso extract of culture medium in which human parathyroid adenomata had been maintained in vitro (Code 72/3). Participants were also asked to include their own house standard.

The participating laboratories were requested to use their own assay procedure to carry out at least two independent assays, using freshly opened ampoules, and including all preparations at several dilutions and in replicate, to assess linearity and parallelism. A range of different immunoassay systems were used including radioimmunoassay, immunoradiometric assay and labelled antibody membrane assay.

The results of this collaborative study showed that the Research Standard was not distinguishable from the other preparations and laboratory working standards of human parathyroid hormone included in the study. It was however shown to be distinguishable from the International Reference Preparation for Parathyroid Hormone, Bovine for Immunoassay.

The mass of native human parathyroid hormone in the Research Standard has been estimated in terms of seven human parathyroid hormone house standards in use in the participants laboratories and the figure given is thus an assumption based on indirect evidence. Participants agreed that the estimated nominal content was equivalent to 25ng of human parathyroid hormone (and is of a similar order of magnitude in terms of the nominal content of the International Reference Preparation of Parathyroid Hormone, Bovine, for Immunoassay) and a potency of 0.025 units has been assigned to the Research Standard for human parathyroid hormone for immunoassay.

11. PARTICIPANTS IN THE COLLABORATIVE STUDY

Dr C. Arnaud, Mayo Clinic, Rochester, Minnesota, USA; Professor G.M. Berlyne, The Soroka Medical Centre, Beer-Sheba, Israel; Dr D.B. Cook and Dr J.H. Dewar, The University and the Royal Victoria Infirmary, Newcastle upon Tyne, UK; Dr P. Desplan and Dr. M.S Moukhtar, Hopital St. Antoine, Paris, France; Dr J.A. Fischer, Orthopadischeklinik, Zurich, Switzerland; Dr J.A. Hendy and Dr. J.L.H. O'Riordan, Middlesex Hospital, London, UK; Dr. R. Hehmann and Dr. R.D. Hesch, Medizinische Hochschule Hanover, Hanover, Germany; Dr.G. Heynen and Dr. P. Franchimont, Hopital de Bavier-Institut de Medicin, University of Liege, Liege, Belgium; Dr C. Hillyard, Endocrine Unit, Royal Postgraduate Medical School, London, UK; Dr. S. Krutziuk, Nichols Institut for Endocrinology, San Pedro, California, USA; Dr P. Lindgreen, Medi-Lab AS, Copenhagen, Denmark; Dr. R. Melick, Royal Melbourne Hospital, Victoria, Australia; Dr T.M. Murray, University of Toronto, Toronto, Canada; Dr M. Peacock, MRC Mineral Metabolism Unit, General Infirmary, Leeds, UK; Mr B. Rafferty and Dr J.M Zanelli, National Institute for Biological Standards and Control, Hampstead, London, UK; Dr G. Segre, Endocrine Unit, Massachusetts General Hospital, Boston, USA; Dr. J.S. Woodhead, Department of Medical Biochemistry, University Hospital, Cardiff, Wales.

12. REFERENCES


13. ACKNOWLEDGEMENTS

The help of the following is gratefully acknowledged. Dr J.S. Woodhead (Cardiff) and Dr. M. Peacock (Leeds) for the material; Dr. P.J. Campbell and his staff (NIBSC) for ampouling the Research Standard; the participants in the collaborative study.

14. 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

15. 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

16. 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.

17. 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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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<tbody>
<tr>
<td>Physical appearance</td>
<td>freeze dried powder</td>
</tr>
<tr>
<td>Corrosive</td>
<td>No</td>
</tr>
<tr>
<td>Stable</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxidising</td>
<td>No</td>
</tr>
<tr>
<td>Hygroscopic</td>
<td>Yes</td>
</tr>
<tr>
<td>Irritant</td>
<td>No</td>
</tr>
<tr>
<td>Flammable</td>
<td>No</td>
</tr>
<tr>
<td>Handling</td>
<td>See caution, Section 2</td>
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<tr>
<td>Other (specify)</td>
<td>Contains material of human origin</td>
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Toxicological properties

<table>
<thead>
<tr>
<th>Effect</th>
<th>Description</th>
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<tbody>
<tr>
<td>Effects of inhalation</td>
<td>Not established, avoid inhalation</td>
</tr>
<tr>
<td>Effects of ingestion</td>
<td>Not established, avoid ingestion</td>
</tr>
<tr>
<td>Effects of skin absorption</td>
<td>Not established, avoid contact with skin</td>
</tr>
</tbody>
</table>

Suggested First Aid

<table>
<thead>
<tr>
<th>Route</th>
<th>Action</th>
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<tbody>
<tr>
<td>Inhalation</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Ingestion</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Contact with eyes</td>
<td>Wash with copious amounts of water. Seek medical advice</td>
</tr>
<tr>
<td>Contact with skin</td>
<td>Wash thoroughly with water.</td>
</tr>
</tbody>
</table>

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.

18. 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.

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19. INFORMATION FOR CUSTOMS USE ONLY

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