Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

International Ref. Preparation
1st IRP Parathyroid Hormone, Human
NIBSC code: 79/500
Instructions for use
(Version 4.0, Dated 04/12/2007)

1. INTENDED USE

At its 26th meeting (1974), the Expert Committee on Biological Standardization of the World Health Organization (ECBS, WHO), noted that immunoassays of human plasma parathyroid hormone were of value in various clinical conditions, and asked the National Institute for Biological Standards and Control, London, in collaboration with interested workers, to obtain material of human origin which could serve as an international reference preparation (IRP). Owing to the scarcity of such material, the Committee particularly emphasized the desirability of internationally collaborative efforts to prepare and characterize the preparation (ECBS 1974).
In December, 1978, a nominal amount of 150µg of hPTH, stated to be more than 95% pure, was donated to WHO as a proposed IRP. The ampouled preparation, code number 79/500, was evaluated by international collaborative study.
The WHO ECBS established the preparation of human parathyroid hormone (hPTH) in ampoules coded 79/500 as the International Reference Preparation (IRP) of Parathyroid Hormone, Human, for Immunoassay. For full details of the ampouled preparation and its collaborative study, see Zanelli & Gaines-Das, 1983.

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.
However, as with all preparations of human origin, this material cannot be assumed to be free from infectious agents. The container and its contents should be used and discarded according to your own laboratory procedures. Such procedures probably will include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening the container to avoid cuts.

3. UNITAGE

By definition, each ampoule contains 0.100 INTERNATIONAL UNITS of hPTH (i.e. 100 MILLI-INTERNATIONAL UNITS).

4. CONTENTS

Country of origin of biological material: United Kingdom.

Human parathyroid hormone approx.	100ng* or 10 picomoles
Albumin (human)	250µg
Lactose	1.25mg

*Note: the estimate of mass of hPTH has been based on indirect evidence obtained from this collaborative study and from the collaborative study carried out to characterize NIBSC Research Standard, ampoule code 75/549 (discussed in Zanelli & Gaines-Das, 1980).

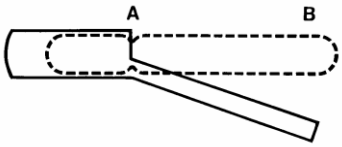
5. STORAGE

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 of the IRP contains the same quantity of the above substances. Dissolve the total contents of the ampoule in a known quantity of a suitable buffer containing 0.2% crystalline albumin, free of protease activity (Caygill, 1977), to minimize the 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 in the freeze dried plug.
For economy in use, particularly in immunoassay, aliquots of a stock solution may be frozen rapidly in dry ice and stored at -40°C for several months. The diluent used for preparation of a stock solution and the stability of such aliquots should be carefully assessed within the assay system in which they are to be used.

8. BULK MATERIAL

The extract of hPTH was made and kindly donated to Dr C D Arnaud (Veterans Administration Hospital, San Francisco, USA) and Dr B Brewer (National Institutes of Health, Bethesda, USA). Parathyroid tissue comprising adenomata and hyperplastic glands was obtained at surgery in Europe and the USA. The tissues were stored at -20°C until the pooled tissue batch was extracted (see Zanelli & Gaines-Das, 1983).

9. DISTRIBUTION INTO AMPOULES

(Procedures as described in Annex 4, 29 WHO Expert Committee on Biological Standardization Report, 1978).
In January, 1979, the frozen solution was defrosted and diluted in 600ml of 0.001M acetic acid in double glass distilled water containing 0.5% lactose (British Drug Houses - Analar grade) and 0.1% re-precipitated human serum albumin (Lister Institute, UK, batch AK3) free from peptidase activity, and sterilised by membrane filtration (Millipore, 0.45µ). Equal amounts (nominally 0.2ml) of the solution were distributed as one batch into approximately 2800 neutral glass ampoules, code numbered 79/500, which were then plunged into liquid nitrogen and lyophilized, the shelf temperature during lyophilization being maintained at -20°C. After secondary desiccation, the ampoules were filled with pure dry nitrogen and sealed by glass fusion. The mean weight of solution in each of 50 weighed ampoules was 0.20386g (variance ± 0.19%, range 0.20223 - 0.20596g).

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The ampoules were tested for leak,s and stored in the dark at -20°C.

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.
Results of assays on the accelerated degradation samples suggested that after storage at 45°C for 2 years, there had been some change in immunoreactivity of 79/500. However, no significant changes were detectable in the preparation after storage at 20°C for 2 years.
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.

11. REFERENCES

Caygill, C.P.J Clin. Chem. Acta, 78, 507-509, 1977
WHO Expert Committee on Biological Standardisation, 26th Report. WHO Tech. Ser. No. 365, Geneva 1975
WHO Expert Committee on Biological Standardisation, 29th Report. WHO Tech. Ser. No. 626, Geneva 1978
WHO Expert Committee on Biological Standardisation, Unpublished Working Document WHO/BS/81/1315, 1981
Zanelli & Gaines Das. J. Endocrinol. 86, 291-304, 1980.
Zanelli & Gaines Das. J. Clin Endocrinol Metab. 57(3), 462-9, 1983.

12. ACKNOWLEDGEMENTS

The help of the following is gratefully acknowledged: Dr C.D Arnaud (San Francisco) and Dr B. Brewer (Bethesda) for donating the highly purified hPTH for the IRP, and for the preparation of 78/551; Dr G. Dorn and Dr R. Montz (Hamburg) for the tissue culture derived preparation for 78/616; Professor R. Ziegler and Dr H. Minne (Heidelberg) for the secondary hyper-parathyroid derived preparation for 78/618; Dr P. J Campbell and his staff (NIBSC) for ampouling all the preparations; the participants in the collaborative study

13. 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

14. 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

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15. 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.

16. 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: Freezed 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.	

17. 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.

18. 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: 2mg
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable**.** **Attached:** No

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