Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Corticotrophin (ACTH), Porcine, For Bioassay
NIBSC code: 59/016
Instructions for use
(Version 4.0, Dated 23/03/2013)

1. INTENDED USE

This consists of a batch of ampoules (coded 59/016) which was established as the Third International Standard for Corticotrophin by the WHO Expert Committee on Biological Standardization in 1962 (WHO ECBS TRS 1963). It was renamed the Third International Standard for Corticotrophin, Porcine, for Bioassay in 1968 (WHO ECBS, TRS 1969). For further details of this Standard and its collaborative study, see Bangham et al (1962). For an assessment of the stability of the Standard and the heterogeneity of the peptides contained in it, see Storring et al (1980).

Several batches of ampoules, **including those in ampoules coded 74/586**, have been prepared in a similar way and from the same material as the International Standard to serve as an International Working Standard for use as national and laboratory standards.

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The material is not of human or bovine origin. 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 contains 5 International Units (by definition)

4. CONTENTS

Country of origin of biological material: United Kingdom.

Each ampoule contains the residue, after freeze-drying, of 1.0ml of a solution which contained:

Porcine ACTH	approx	50 µg
Lactose	"	5 mg
Acetic acid	"	3 mg

Nitrogen gas at slightly less than atmospheric pressure.

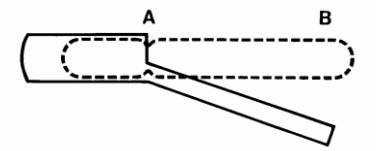
5. STORAGE

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 practical purposes each ampoule contains the same amount of the same materials. Dissolve all the contents in a known amount of buffer solution. No attempt should be made to weigh portions of the freeze-dried powder.

For economy of use the solution can be kept for several months if an anti-bacterial preservative is added and the solution is subdivided into several small containers, which are frozen rapidly to below -70°C and then stored below -30°C in the dark; repeated freezing and thawing should be avoided. If extensive dilutions are prepared, a carrier protein (0.1% w/v) should be added, which is free of peptidase.

The material has not been sterilized and contains no bacteriostat

8. STABILITY

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.

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.

9. REFERENCES

Bangham DR, Mussett MV & Stack-Dunne MP (1962). Bull Wld Hlth Org, 27, 395-408.

Storring PL, Gaines Das RE, Tiplady RJ, Stenning BE & Mistry Y (1980). J. Endocrinol., 85, 533-539.

WHO Expert Committee on Biological Standardization. 15th Report. World Health Organization Technical Report Series No. 259, (1963), 13.

WHO Expert Committee on Biological Standardization. 21st Report. World Health Organization Technical Report Series No. 413, (1969), 15

10. ACKNOWLEDGEMENTS

Grateful acknowledgements are due to the Armour Company of Great Britain and the United States Pharmacopeia for providing the material for the Standard and to the participants in the international collaborative study.

11. 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

PREPARATION OF AMPOULES

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WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

The bulk material. This consisted of 4.5g of a batch of corticotrophin made by the Armour Laboratories, Chicago, and generously donated by the Armour Company of Great Britain, and a further 4.5g of material from the same manufacturing batch that were supplied through the courtesy of the United States Pharmacopeia. The material was made from pig pituitaries and purified by glacial acetic acid extraction, ethyl ether precipitation, oxycellulose adsorption and elution, removal of electrolytes by ion exchange, and freeze-drying. Its stated potency was 99.9 IU/mg by subcutaneous Sayers' assay and 31.8 - 34.5 IU/mg by intravenous Sayers' assay.

ACTIVITY OF AMPOULE CONTENTS

This was compared with the activity of the Second International Standard in an international collaborative study (Bangham et al, 1962). The pressor activity, estimated by rat blood pressure assay in terms of the Third International Standard for Oxytocin and Vasopressin, Ovine, for Bioassay, was found to be <25miu/ampoule. Accelerated thermal degradation studies have shown the Standard to be very stable under normal storage conditions (Storring et al, 1980).

12. 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

13. 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.

14. 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): none	
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.	

15. 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.

16. 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: 8mg
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.