Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO Reference Reagent
Human Chorionic Gonadotrophin, Alpha Subunit (Purified)
NIBSC code: 99/720
Instructions for use
(Version 5.0, Dated 12/06/2019)

1. INTENDED USE

This consists of a batch of lyophilised ampoules containing the alpha subunit of human chorionic gonadotrophin, purified to remove other forms of human chorionic gonadotrophin, including hCG, β subunits and nicked forms. The preparation was established as the first WHO Reference Reagent at the 2001 meeting of the Expert Committee on Biological Standardization.
In making this recommendation the committee noted that the preparation 99/720 is not intended to replace the existing International Standard for hCG-α as the primary calibrant for immunoassays, but is intended for use in investigating and characterizing the specificity of existing hCG and hCG- α assays.

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 in opening ampoules or vials, to avoid cuts.

3. UNITAGE

0.84nmol/ampoule, by definition

The nmol value of 99/720 is assigned without uncertainty. Where required, the uncertainty of the ampoule content of 99/720 may be considered to be the coefficient of variation of the fill volume, which was determined to be 0.17%.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Lyophilised residue containing approximately 1.0 nmol purified alpha subunit of human chorionic gonadotrophin (hCG-α), 2 mg human serum albumin, phosphate buffer salts (50mM pH7.4)

5. STORAGE

Unopened ampoules should be stored at –20ºC **Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.**

6. DIRECTIONS FOR OPENING

DIN ampoules have an 'easy-open' coloured stress point, where the narrow ampoule stem joins the wider ampoule body. Various types of ampoule breaker are available commercially. To open the ampoule, tap the ampoule gently to collect material at the bottom (labelled) end and follow manufactures instructions provided with the ampoule breaker.

7. USE OF MATERIAL

For practical purposes each ampoule contains the same quantity of HCG-α. The entire content of each ampoule should be completely dissolved in an accurately measured amount of buffer solution. No attempt should be made to weigh out portions of the freeze-dried powder. The use of water to reconstitute ampoule contents is not recommended. The material has not been sterilized and the ampoules contain no bacteriostat.

VALUE ASSIGNMENT BY COLLABORATIVE STUDY

The molar content of this preparation was assigned through an international collaborative study involving 11 laboratories in 5 countries. Value assignment of 99/720 was achieved through (i) determination of the molar concentration of a concentrated stock solution by amino acid analysis (ii) using the assigned concentration of the concentrated stock solution to estimate the molar content of the diluted, pre-lyophilised formulation and (iii) correcting this value for the mean percentage loss of immunoreactivity upon freeze drying.
By this process, the content of 99/720 was defined as 0.84 nmol/ampoule.
The preparation exhibited no significant loss of immunoreactivity upon storage at elevated temperatures and is considered stable.

For further details of this material, please see:
Bristow, AF, Sturgeon, C. and the IFCC Working Group for hCG (2001) Report of an International Collaborative Study to Evaluate Candidate WHO International Standards for six molecular forms of human Chorionic Gonadotrophin. WHO External Committee on Biological Standardization BS/01.1944 WHO, Geneva, Switzerland.

Bristow AF et al., (2005) Establishment, value assignment and characterization of new WHO Reference Reagents for six molecular forms of human Chorionic Gonadotrophin. Clin. Chem. 51, 177-182.

Birken S et al., (2003) Preparation and characterization of new WHO Reference Reagents for human chorionic gonadotrophin and metabolites. Clin. Chem. 49, 144-154.

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. 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

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

10. 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

11. 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.

12. 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: White lyophilised powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify): Can react with oxidising materials. Avoid contact with acids and alkalis.	
Toxicological properties	
Effects of inhalation: No adverse effects have been reported for this material.	
Effects of ingestion: No adverse effects have been reported for this material.	
Effects of skin absorption: No adverse effects have been reported for this material.	
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.	

13. 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.

14. 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: 3mg
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.