Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
6th International Standard for Chorionic Gonadotrophin, human
NIBSC code: 18/244
Instructions for use
(Version 1.0, Dated 12/11/2020)

1. INTENDED USE

The WHO International Standard for human chorionic gonadotrophin (hCG) is intended for use in the calibration of bioassays and immunoassays for hCG. This preparation, coded 18/244, contains highly purified intact hCG, and was ampouled and evaluated for its suitability to serve as a WHO International Standard in a collaborative study. It was established as the 6th International Standard by the Expert Committee on Biological Standardization of the WHO at its 71st meeting in October 2020. It replaces the 5th International Standard for hCG, coded 07/364.

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

Each ampoule of 18/244 contains:
159 IU per ampoule for bioassay
186 IU per ampoule for immunoassay, corresponding to 0.41 nmol per ampoule for immunoassay. This value has an expanded uncertainty of 0.40 - 0.43 nmol/amp (k=2.12).

4. CONTENTS

Country of origin of biological material: USA (purified hCG), Italy (human plasma albumin).
Each ampoule contains the residue after freeze-drying of 0.5 mL of a solution that contained:
20 µg hCG
10 mg/ml trehalose
50 mM sodium phosphate buffer, pH 7.4
2 mg/ml human plasma albumin

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

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution
For all practical purposes, each ampoule contains the same quantity of the substances listed above. Depending upon intended use, dissolve the total contents of the ampoule in a known volume of a suitable diluent. Carrier protein (0.05 - 0.1% BSA or HSA) should be added where extensive dilution is required. The ampoules do not contain bacteriostat and the solution of the reagent should not be assumed to be sterile.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

The stability of this International Standard was assessed via an accelerated thermal degradation (ATD) study, in which ampoules of 18/244 stored at elevated temperatures (4, 20, 37 and 45 ºC) for 7 months were analysed by immunoassay. No significant losses of potency were observed in samples stored at elevated temperatures relative to the reference storage temperature of -20ºC. It was therefore not possible to predict the long-term stability of the material at storage temperatures of -20ºC. However, the lack of observed degradation indicates that the material is highly stable.

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 internatinoal 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. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES

This standard was produced under guidelines cited in the WHO Technical Report Series, No. 932, 2006, Annex 2.

Details of the collaborative study can be found in the following publication:
Moore, M., Partridge, K., Cowper, B., Rigsby, P. and Burns, C. (2020) Proposed 6th International Standard for human chorionic gonadotrophin. WHO/BS/2020.2395. *Expert Committee on Biological Standardization, 19-23 October 2020*. https://www.who.int/publications/m/item/WHOBS2020.2395

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of all the participants in the collaborative study, the IFCC for their kind donation of the bulk hCG, and the Centre for Biological Reference Materials, NIBSC, for the preparation and dispatch of the ampouled materials.

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

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

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

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: White powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	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.

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: 10 mg
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.

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