WHO International Standard

5th WHO IS
Chorionic Gonadotrophin
NIBSC code: 07/364
Instructions for use
(Version 3.0, Dated 06/04/2013)

1. INTENDED USE
The 4th International Standard was widely used for the calibration of
assays to control the quality and potency of chorionic gonadotrophin (CG)
used in the treatment of infertility in women and sometimes in men, and
for the calibration of assays used in the diagnosis of pregnancy and a
range of other clinical conditions. In 2006 it became apparent that stocks
of the 4th IS were becoming exhausted and as a result, the WHO Expert
Committee on Biological Standardisation (ECBS) recognised the need for
a replacement International Standard. The 5th IS for Chorionic
Gonadotrophin (07/364) was established at the 60th Meeting of the
ECBS. This material replaces the 4th IS, which is discontinued.

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
This preparation has dual unitage.

Each ampoule contains 179 INTERNATIONAL UNITS for the calibration
of immunoassays. For those users wishing to calibrate immunoassays in
molar units, the preparation has also been assigned a unitage in molar
terms of 0.39 nmol per ampoule.

For the purposes of calibrating bioassays to control therapeutic
preparations of CG, each ampoule contains 162 INTERNATIONAL
UNITS per ampoule, based on the mean potency calculated in the
collaborative study from bioassay estimates alone.

4. CONTENTS
Country of origin of biological material: United Kingdom.
Each ampoule contains the residue after freeze-drying of 1ml of a solution
that contained:

chorionic gonadotrophin
2 mg/ml human serum albumin
50 mM sodium phosphate pH 7.4
10 mg/ml trehalose

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
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 practical purposes each ampoule contains the same quantity of human
chorionic gonadotrophin. The entire content of each ampoule should be
completely dissolved in an accurately measured amount of buffer solution.
The use of water to reconstitute ampoule contents is not recommended. The
material has not been sterilized and the ampoules contain no bacteriostat.

COLLABORATIVE STUDY
The preparation was evaluated in a collaborative study carried out in 19
laboratories in 11 countries, organised with the following aims:

1) to calibrate the preparation of intact CG by immunoassay and bioassay
for use as a potential International Standard.
2) to assess the stability of the proposed International Standard after
accelerated thermal degradation.

By comparison with the 4th IS for CG (75/589), the mean potency calculated
from immunoassay estimates for 07/364 was 179.1 IU per ampoule. The
mean potency calculated from bioassay estimates for 07/364 was 162 IU per
ampoule. Comparisons with the 1st WHO Reference Reagent (99/688) by
immunoassay demonstrated that 07/364 contained 0.39 nmol per ampoule.

The candidate preparation 07/364 is sufficiently stable to serve as an
International Standard since no significant loss in immunoreactivity or
bioactivity was found at any of the elevated temperatures. This suggests that
07/364 is likely to be highly stable under long term storage conditions at
-20°C.

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

9. REFERENCES

10. ACKNOWLEDGEMENTS
We gratefully acknowledge the important contributions of all the participants
and the International Federation of Clinical Chemistry and Laboratory
Medicine who kindly donated the purified intact hCG.

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
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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical appearance:</strong> White powder</td>
</tr>
<tr>
<td><strong>Corrosive:</strong> No</td>
</tr>
<tr>
<td><strong>Stable:</strong> Yes</td>
</tr>
<tr>
<td><strong>Oxidising:</strong> No</td>
</tr>
<tr>
<td><strong>Hygroscopic:</strong> Yes</td>
</tr>
<tr>
<td><strong>Irritant:</strong> No</td>
</tr>
<tr>
<td><strong>Flammable:</strong> No</td>
</tr>
<tr>
<td><strong>Handling:</strong> See caution, Section 2</td>
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<tr>
<td><strong>Other (specify):</strong> Can react with oxidising materials. Avoid contact with acids and alkalis.</td>
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<tr>
<th>Toxicological properties</th>
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<tr>
<td><strong>Effects of inhalation:</strong> Not established, avoid inhalation</td>
</tr>
<tr>
<td><strong>Effects of ingestion:</strong> Not established, avoid ingestion</td>
</tr>
<tr>
<td><strong>Effects of skin absorption:</strong> Not established, avoid contact with skin</td>
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</tbody>
</table>

**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

<table>
<thead>
<tr>
<th>Country of origin for customs purposes*: United Kingdom</th>
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<tbody>
<tr>
<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: 12mg</td>
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<tr>
<td>Toxicity Statement: Non-toxic</td>
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<tr>
<td>Veterinary certificate or other statement if applicable. Attach: No</td>
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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_biol_esstandardsrev2004.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.