Non WHO Reference Material
Insulin-Like Growth Factor Binding Protein-3
NIBSC code: 93/560
Instructions for use
(Version 4.0, Dated 21/01/2008)

This material is not for in vitro diagnostic use.

1. INTENDED USE

This consists of a batch of ampoules (coded 93/560) containing non-
glycosylated recombinant DNA-derived insulin-like growth factor binding
protein-3 (rhIGFBP-3) expressed in E. coli. In an international
collaborative study designed to compare the ampouled preparation of
rhIGFBP-3 with local standards, apparent differences were detected in
several systems, most of which involved comparisons with glycosylated
house standards. However there was broad agreement among a number of
participants that the ampoule contents were approximately 3.5ug, particularly from those assays which were homologous for E. coli-derived
IGFBP-3. Because the range of estimates obtained for the ampoule
content of the non-glycosylated material indicated that it would not be
suitable to serve as a standard in some immunoassay and bioassay
systems, the preparation is intended solely for use as a research reagent.

2. CAUTION

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

The material is of bovine origin. The material is certified to be obtained
from animals taken from a closed herd in the female line since 1980, in
which no animal has been clinically suspected of having BSE & which
has not been fed rations containing ruminant derived protein during
that period. 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 material is issued on the understanding that it has no official status
and has no definitive unitage or content ascribed to it.

4. CONTENTS

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

- Recombinant DNA-derived IGFBP-3: approximately 3.5ug
- Bovine serum albumin: 1.0mg
- 0.02M sodium phosphate pH 6.0

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. Tap the
ampoule gently to collect the material at the bottom (labelled)
end. Ensure that the disposable ampoule safety breaker provided is
pushed down on the stem of the ampoule and against the shoulder of
the ampoule body. Hold the body of the ampoule in one hand and the
disposable ampoule breaker covering the ampoule stem between the
thumb and first finger of the other hand. Apply a bending force to open
the ampoule at the coloured stress point, primarily using the hand holding
the plastic collar.

Care should be taken to avoid cuts and projectile glass fragments that
might enter the eyes, for example, by the use of suitable gloves and an
eye shield. Take care that no material is lost from the ampoule and no
glass falls into the ampoule. Within the ampoule is dry nitrogen gas at
slightly less than atmospheric pressure. A new disposable ampoule
breaker is provided with each DIN ampoule.

7. USE OF MATERIAL

For practical purposes each ampoule contains the same quantity of IGFBP-
3. The entire contents 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.

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. For information specific to a particular
biological standard, contact standards@nibsc.ac.uk.

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

9. ACKNOWLEDGEMENTS

Grateful acknowledgements are due to Celtrix Pharmaceuticals for providing
the material, the staff of CBRM for ampouling the preparation and the
participants in the collaborative study.

10. 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

11. 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
12. 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.

13. 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>
<th></th>
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<tbody>
<tr>
<td>Physical appearance: White lyophilised powder</td>
<td>Corrosive: No</td>
</tr>
<tr>
<td>Stable: Yes</td>
<td>Oxidising: No</td>
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<tr>
<td>Hygroscopic: Yes</td>
<td>Irritant: No</td>
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<tr>
<td>Flammable: No</td>
<td>Handling: See caution, Section 2</td>
</tr>
</tbody>
</table>

| Other (specify): | Contains material of mammalian origin. Can react with oxidising materials. Avoid contact with acids and alkalis. |

<table>
<thead>
<tr>
<th>Toxicological properties</th>
<th></th>
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<tbody>
<tr>
<td>Effects of inhalation:</td>
<td>Not established, avoid inhalation</td>
</tr>
<tr>
<td>Effects of ingestion:</td>
<td>Not established, avoid ingestion</td>
</tr>
<tr>
<td>Effects of skin absorption:</td>
<td>Not established, avoid contact with skin</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Suggested First Aid</th>
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<tbody>
<tr>
<td>Inhalation:</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Ingestion:</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Contact with eyes:</td>
<td>Wash with copious amounts of water. Seek medical advice</td>
</tr>
<tr>
<td>Contact with skin:</td>
<td>Wash thoroughly with water.</td>
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</table>

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<thead>
<tr>
<th>Action on Spillage and Method of Disposal</th>
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<tr>
<td>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.</td>
<td></td>
</tr>
</tbody>
</table>

14. 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.