WHO International Standard
2nd International Standard for Fibrinogen Plasma
NIBSC code: 98/612
Instructions for use
(Version 4.0, Dated 01/04/2008)

1. INTENDED USE
The 2nd International Standard for Fibrinogen in plasma was established by the Expert Committee on Biological Standardisation of the World Health Organization in October 1999. The preparation consists of ampoules (coded 98/612) each containing 1 ml aliquots of solvent/detergent treated pooled human plasma, freeze-dried.

This standard is intended to be used in the measurement of fibrinogen in plasma and is primarily intended for calibration of secondary and/or in-house working standards of fibrinogen plasma.

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
The Fibrinogen content of the standard was determined by comparison against the 1st IS Fibrinogen plasma (89/644) in an international collaborative study involving 11 laboratories in 6 countries. All laboratories used the automated Clauss procedure for the estimation of Fibrinogen. The overall mean potency assigned to the 2nd IS is:

2.2 mg Fibrinogen per ml
(after reconstitution by the addition of 1ml distilled water)

4. CONTENTS
Country of origin of biological material: United Kingdom.
The 2nd International Standard was prepared from solvent/detergent treated pooled normal plasma. Twenty one packs from a single manufacturing lot (812039950) were thawed and pooled to give 4.2 litres of plasma. The plasma was kept at room temperature throughout distribution into approximately 4,000 ampoules, then freeze-dried and dried material. The mean liquid filling weight of 77 checkweight ampoules was 1.0061 g (range 1.0045-1.0085 g) with a coefficient of variation of 0.069%. Estimates of residual moisture after freeze-drying and secondary desiccation gave a mean value of 0.304%.

5. STORAGE
Unopened ampoules should be stored at -20°C. After reconstitution, any unused material must be discarded, not frozen for further use.

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 (labeled) end. Ensure that the disposable ampoule safety breaker 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
Ampoules should be warmed to room temperature before reconstitution. Dissolve the total contents of each ampoule by adding 1.0 ml of distilled water, using gentle shaking, then transfer the contents to a stoppered plastic tube. Do not attempt to weigh out any portion of the freeze-dried material.

Store the reconstituted standard at room temperature and use within four hours. The reconstituted standard should only be used freshly and must not be frozen for subsequent use.

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.

Accelerated degradation studies have indicated that the 2nd International Standard Fibrinogen plasma is extremely stable when stored at -20°C. Predictions for the loss of Fibrinogen (Clauss method), when stored at -20°C, were below 0.01% per year.

NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

10. ACKNOWLEDGEMENTS
Are made to Octapharma Ltd., Coventry, UK, for kindly supplying the solvent/detergent treated frozen plasma and to the participants in the collaborative study for their efforts in carrying out the calibration assays.

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

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...
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

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical appearance</td>
<td>Freeze dried powder</td>
</tr>
<tr>
<td>Stable</td>
<td>Yes</td>
</tr>
<tr>
<td>Hygroscopic</td>
<td>Yes</td>
</tr>
<tr>
<td>Flammable</td>
<td>No</td>
</tr>
<tr>
<td>Corrosive</td>
<td>No</td>
</tr>
<tr>
<td>Oxidising</td>
<td>No</td>
</tr>
<tr>
<td>Irritant</td>
<td>No</td>
</tr>
<tr>
<td>Handling</td>
<td>See Caution (Section 2)</td>
</tr>
<tr>
<td>Contains material of human origin</td>
<td></td>
</tr>
</tbody>
</table>

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: 0.08g
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_biol_efstandardsrev2004.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.