WHO International Standard
3rd INTERNATIONAL STANDARD FIBRINOGEN PLASMA
NIBSC code: 09/264
Instructions for use
(Version 1.0, Dated 25/11/2011)

1. INTENDED USE
The WHO 3rd International Standard for Fibrinogen Plasma, consists of
glass ampoules, coded 09/264, containing 1ml aliquots of a freeze-dried
solvent-detergent treated pooled normal human plasma. This preparation
was established by the Expert Committee on Biological Standardization of
the World Health Organization in October 2011 and details of the
preparation and value assignment are available in document
WHO/BS/2011.2168. 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 WHO 3rd International Standard was calibrated in an international
collaborative study involving 21 laboratories in 11 countries. A potency of

2.7 mg per ampoule

has been assigned. This figure is based on comparison with the 2nd
International Standard for Fibrinogen Plasma, using primarily Clauss
assays.

4. CONTENTS
Country of origin of biological material: United Kingdom
The WHO 3rd International Standard for Fibrinogen Plasma, consists of
aliquots of a freeze-dried solvent-detergent treated pooled normal
human plasma and was prepared at the National Institute for Biological
Standards and Control (NIBSC) in January 2010.
After thawing of 50 units (10,000 ml) of the product, this material was
pooled and kept on ice prior to being filled and freeze-dried in sealed
glass ampoules at NIBSC, under conditions required for International
Standards1. One ml of this material was dispensed into each of
approximately 10,000 ampoules. The mean filling weight was 1.0080 g
(range 1.0020 g to 1.0150 g) and the coefficient of variation (CV) was
0.18% based on 396 check-weight samples. Mean residual moisture
after freeze-drying was 0.34% (CV 24.8%, n=12) and mean oxygen
headspace was 0.29% (CV 32.2%, n=12).

5. STORAGE
Unopened ampoules should be stored in the dark at -20°C. After
reconstitutions any unused material must be discarded, not frozen for later
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 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
The total contents of the ampoule should be reconstituted at room
temperature with 1 ml distilled water, dissolved by gentle swirling to avoid
froth and transferred immediately to a suitable plastic tube. No attempt
should be made to weigh out any portion of the freeze-dried material.

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.
In common with previous WHO Plasma Standards for blood coagulation
factors, it is recommended that the standard is transferred, after
reconstitution, to a plastic tube and if stored on melting ice, the standard
should be used within 3 hours of reconstitution.

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

9. REFERENCES
1. Campbell P J. Procedures used for the production of biological standards

10. ACKNOWLEDGEMENTS
The contributions of all the participants in the study are gratefully
acknowledged. We are grateful to our colleagues in the Standards
Processing Division and Process Development Section, NIBSC, for
ampouling and processing the candidate and trial preparations and for
the dispatch of collaborative study samples to participants. We are
grateful to Kedrion S.p.A. (Italy) and Octapharma (Austria) for their kind
donation of materials for the study. We further like to thank the
ISTH/SSC Fibrinogen and Factor XIII Subcommittee for their support.

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.bipm.org/en/committees/jc/jctlm/
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 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>
<th></th>
</tr>
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<tbody>
<tr>
<td>Physical appearance: Frozen dried powder</td>
<td>Corrosive: No</td>
</tr>
<tr>
<td>Stable: Yes</td>
<td>Oxidising: No</td>
</tr>
<tr>
<td>Hygroscopic: Yes</td>
<td>Irritant: No</td>
</tr>
<tr>
<td>Flammable: No</td>
<td>Handling: See Caution (Section 2)</td>
</tr>
<tr>
<td>Other (specify): 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 |
| 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. 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.