WHO International Standard
1st INTERNATIONAL STANDARD FOR FACTOR VII
CONCENTRATE
NIBSC code: 97/592
Instructions for use
(Version 3.0, Dated 04/03/2008)

1. INTENDED USE
The 1st International Standard for Factor VII, Concentrate consists of ampoules (coded 97/592) containing 1ml aliquots of a human plasma-derived FVII concentrate, freeze-dried. This preparation was established by the Expert Committee on Biological Standardisation of the World Health Organisation in October 1998 and a potency of 6.3 International Units has been assigned to each ampoule.

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

Each individual plasma donation and the final freeze-dried product was tested for HBsAg and for antibodies to HCV and HIV 1 and 2 and found to be negative. The freeze-dried standard has also been tested and found negative for HCV RNA by PCR. 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 1st International Standard was calibrated for FVII activity in an international collaborative study involving 16 laboratories from 10 countries by assay against the 2nd IS Factors II, VII, IX, X, plasma (94/746) and against fresh pools of normal plasma, using clotting and chromogenic methods. The assigned activity for use with both one-stage clotting and chromogenic assay methods is 6.3 IU per ampoule.

4. CONTENTS
Country of origin of biological material: United Kingdom.
The bulk material used to prepare the 1st International Standard was purified from pooled human plasma using techniques which included ion exchange chromatography. Viricidal treatment involved exposure to solvent/detergent. The 1st International Standard was prepared in September 1997 from 33 vials of freeze-dried Factor VII concentrate. Vials were reconstituted with distilled water, as described by the manufacturer, and further diluted in buffer (Tris 50 mM, sodium chloride 150 mM, Trehalose 5mg/ml, human albumin 12.5 mg/ml pH 7.4) to a final volume of 3.1 litres.

The solution was kept at 4°C during distribution into approximately 3,000 ampoules, then freeze-dried under conditions used for International Biological Standards (1). The mean liquid filling weight from 61 checkweigh ampoules was 1.0104 g (range 1.0057 to 1.0138 g) with a coefficient of variation of 0.14%. Estimates of residual moisture after freeze-drying and secondary desiccation gave a mean value of 0.056%.

5. STORAGE
Unopened ampoules should be stored in the dark at -20°C or below. 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
No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution
Reconstitute the total contents of each ampoule of the Standard at room temperature with 1.0 ml of distilled water, using gentle shaking. Transfer the solution to a plastic tube and keep on ice; the standard is stable for use within two hours of reconstitution.

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.

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

9. REFERENCES

10. ACKNOWLEDGEMENTS
The efforts of the participants in the collaborative study are gratefully acknowledged. The following manufacturers are acknowledged for the supply of candidate materials from which the International Standard was selected: Laboratoires de Fraccionnement et Biotechnologies (LFB); Lille, France; Bio Products Laboratory (BPL), Elstree, UK.

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 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>
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<tbody>
<tr>
<td>Physical appearance: Solid</td>
<td></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>Other (specify):</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Toxicological properties</th>
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<tr>
<td>Effects of inhalation:</td>
<td></td>
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<tr>
<td>Effects of ingestion:</td>
<td></td>
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<tr>
<td>Effects of skin absorption:</td>
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**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 spills should be treated as biological waste.

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: 0.031 g

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 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.

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.