Working Standard
6th British Working Standard for
Blood Coagulation Factors II, IX, X Concentrate
NIBSC code: 07/326
Instructions for use
(Version 2.0, Dated 12/07/2013)

This material is not for in vitro diagnostic use.

1. INTENDED USE
The 6th British Working Standard for Blood Coagulation Factors II, IX, X Concentrate, was established by the National Institute for Biological Standards and Control in January 2009. This batch of standard, consists of ampoules (coded 07/326) containing aliquots of freeze-dried blood coagulation factors II, IX, X, concentrate, is intended for the calibration of coagulation factors II, IX and X functional activity in therapeutic concentrates.

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 standard was calibrated for coagulation factors II, IX, X in a collaborative study involving 7 expert laboratories. Potencies were assigned against the 4th International Standard for Blood Coagulation Factor IX, Concentrate, 07/182 and the 3rd International Standard for Blood Coagulation Factors II and X Concentrate, 98/590. The assigned potencies after reconstitution with 0.5 ml of distilled water are:

- FIL: 8.6 IU/ml; *GCV = 2.4%
- FIX: 9.8 IU/ml; GCV = 3.5%
- FX: 7.2 IU/ml; GCV = 4.9%

*GCV = Geometric Coefficient of Variation

4. CONTENTS
Country of origin of biological material: United Kingdom.
The standard, 07/326, was prepared at the National Institute for Biological Standards and Control in June 2008. The liquid bulk in 50mM Tris, 150mM NaCl, 2 mg/ml Trehalose, 5mg/ml human albumin, pH 7.4 buffer, was kept between 2 - 8°C throughout the distribution into approximately 10,000 ampoules. The mean liquid fill weight was 0.5053g, with a coefficient of variation of 0.29%

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.

Allow the ampoule to equilibrate at room temperature for 10 minutes. Reconstitute the total content with 0.5 ml distilled water using gentle agitation. Transfer the content to a plastic tube. Assays should be carried out as soon as possible upon reconstitution. It is not recommended to freeze-thaw aliquots after reconstitution 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.

NIBSC follows the policy of WHO with respect to its reference materials. It is the policy of WHO not to assign expiry dates to international reference materials. They remain valid with the assigned potency and status until withdrawn or amended.

Accelerated degradation studies, using ampoules stored at elevated temperatures relative to ampoules stored at -150°C, have shown that the 6th British Working Standard is very stable in unopened ampoules stored at -20°C. The predicted loss of activity is less than 0.01% per year for all measured parameters. The accelerated degradation study and real time monitoring will continue for the lifetime of the standard.

9. REFERENCES
Not applicable.

10. ACKNOWLEDGEMENTS
We are grateful to the participants of the collaborative study, Bio Products Laboratory, Elstree, United Kingdom for the generous donation of the candidate material.

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/standardisation/international_standards.aspx
NIBSC Terms & Conditions:
http://www.nibsc.org/terms_and_conditions.aspx

NIBSC
Confidence in Biological Medicines
Medicines & Healthcare products
Regulatory Agency
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>
</thead>
<tbody>
<tr>
<td>Physical appearance:</td>
<td>Corrosive: No</td>
</tr>
<tr>
<td>White freeze-dried powder</td>
<td></td>
</tr>
<tr>
<td>Stable:</td>
<td>Oxidising: No</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Hygroscopic:</td>
<td>Irritant: Unknown</td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Flammable:</td>
<td>Handling: See caution, Section 2</td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Other (specify):</td>
<td>Material of human origin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicological properties</th>
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</tr>
</thead>
<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>
</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 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*:</th>
<th>United Kingdom</th>
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</thead>
<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>
<td></td>
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<tr>
<td>Net weight:</td>
<td>0.013g</td>
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<tr>
<td>Toxicity Statement:</td>
<td>Toxicity not assessed</td>
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<tr>
<td>Veterinary certificate or other statement if applicable.</td>
<td></td>
</tr>
<tr>
<td>Attached:</td>
<td>No</td>
</tr>
</tbody>
</table>

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WHO International Laboratory for Biological Standards, 
UK Official Medicines Control Laboratory