



**WHO International Standard**  
**The 1st International Standard for Activated Blood Coagulation**  
**Factor XI (FXIa), Human**  
**NIBSC code: 13/100**  
**Instructions for use**  
**(Version 1.0, Dated 19/02/2015)**

### 1. INTENDED USE

The 1st International Standard for Activated Blood Coagulation Factor XI (FXIa), Human, is intended for quantification of FXIa activity in therapeutic products. This preparation was established as an International Standard by the Expert Committee on Biological Standardisation (ECBS) of the World Health Organization (WHO) in October 2014, with a label potency of 9.8 IU/ampoule.

The ECBS report numbered WHO/BS/2014.2245 is available from WHO. [http://apps.who.int/iris/bitstream/10665/137475/1/WHO\\_BS\\_2014.2245\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/137475/1/WHO_BS_2014.2245_eng.pdf?ua=1).

### 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

Value assignment was relative to the WHO International Reference Reagent for Activated Blood Coagulation Factor XI (FXIa), Human, 11/236, by chromogenic functional activity assays which were based on the conversion of FIX to FIXa by FXIa.

The labelled potency is 9.8 IU/ampoule.

FOR INFORMATION ONLY: Molar concentration was determined in one laboratory, by active site titration of the bulk starting material against the fluorimetric titrant, 4-methylumbelliferyl-4-guanidinobenzoate hydrochloride hydrate (MUGB), extrapolated to the final ampoule as 8.8 nM.

### 4. CONTENTS

Country of origin of biological material: USA.

A single batch of purified human FXIa (11,500 u/mg relative to the International Reference Reagent) was diluted in 50 mM Tris, 150 mM NaCl, 5 mg/ml trehalose and 0.5% human serum albumin to approximately 10 u/ml. The material was then distributed in approximately 18,000 glass DIN ampoules, coded 13/100 and freeze-dried under the conditions employed for international biological standards<sup>1</sup>. The mean weight of liquid content of 698 check weight ampoules was 1.0078g, with coefficient of variation of 0.15%. The mean residual moisture was 0.15% (n = 12) and the mean head space oxygen was 0.19% (n = 12).

### 5. STORAGE

Unopened ampoules should be stored in the dark at or below -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. Various types of ampoule breaker are available commercially. To open the ampoule, tap the ampoule gently to collect material at the bottom (labelled) end and follow manufactures instructions provided with the ampoule breaker.

### 7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution

Allow the ampoules to warm up to room temperature. Taking care to ensure that all material is in the lower part of the ampoule. Open ampoule as directed. Reconstitute with 1.0 ml of distilled water and transfer contents to a plastic tube. The reconstituted material should be used as soon as possible.

### 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. Accelerated degradation studies, which involved testing samples stored at elevated temperature against samples stored at below -150°C, have shown that the 1st International Standard is stable in unopened ampoules when stored at -20°C or below<sup>2</sup>. The predicted loss of activity is <0.001% of the original potency per year when stored at -20°C. The assigned value remains valid until the material is replaced or withdrawn.

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

Once reconstituted, the product will remain stable for 3 hours when stored in a plastic container on melting ice.

### 9. REFERENCES

1. Campbell PJ. International biological standards and reference preparations: procedures used for the production of biological standards and reference materials. *Journal of Biogocial Standardization* 1974; 2, 259.

2. Kirkwood TBL. Predicting the stability of biological standards and products. *Biometrics* 1977; 33, 736.

### 10. ACKNOWLEDGEMENTS

Participants of the collaborative study.

### 11. FURTHER INFORMATION

Further information can be obtained as follows;

This material: [enquiries@nibsc.org](mailto: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](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](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](mailto: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

Physical and Chemical properties	
Physical appearance: white freeze-dried solid	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: Unknown
Flammable: No	Handling: See caution, Section 2
Other (specify): contain material of human origin	
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](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

<b>Country of origin for customs purposes*:</b> 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.
<b>Net weight:</b> 0.0248g
<b>Toxicity Statement:</b> Toxicity not assessed
<b>Veterinary certificate or other statement</b> if applicable.
<b>Attached:</b> 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](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.