



WHO International Standard
The 4th IS for Blood Coagulation Factors II and X Concentrate
NIBSC code: 11/126
Instructions for use
(Version 1.0, Dated 27/06/2013)

1. INTENDED USE

The 4th International Standard for Factors II and X, Concentrate, consists of ampoules, coded 11/126, containing aliquots of a freeze-dried concentrate prepared from human plasma. This preparation was established as the 4th International Standard for Factors II and X, Concentrate, by the Expert Committee on Biological Standardisation of the World Health Organisation in October 2012. This preparation is intended for FII and X potency estimates in Factor IX and prothrombin complex 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 by 28 laboratories in 14 countries against the 3rd International Standard for Factors II and X, Concentrate (98/590). Functional assays performed were based on snake venom chromogenic methods, prothrombin time clotting assays and APTT clotting assays, using the appropriate clotting factor deficient plasma (Factor II or Factor X deficient plasma). The assigned potencies are as follows:

Factor II: 9.4 IU/ampoule
Factor X: 8.1 IU/ampoule

4. CONTENTS

Country of origin of biological material: United Kingdom.
The single batch of material was diluted in 40 mM Tris, 120 mM NaCl, 1.6 mg/ml trehalose and 4 mg/ml human serum albumin. pH 7.4. The material was distributed in glass ampoules, filled and freeze-dried according to guidelines for production of international standards (1). All material had been tested and was found negative for anti-HIV1/2, HBsAg and anti-hepatitis C. The mean weight of liquid content of 587 check weight ampoules was 1.0074g, with a coefficient of variation of 0.14%. The mean weight of the freeze-dried plug was 25.5 mg, with a coefficient of variation of 0.84%. The mean residual moisture was 0.69%.

5. STORAGE

Unused material must be discarded and not frozen for later use. Unopened ampoules should be stored 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 manufacturers 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 ampoules to warm to room temperature. Open ampoule, taking care to ensure that all material is in the lower part, and reconstitute with 1.0 ml distilled water. The reconstituted Standard should be used as soon as possible, and within three hours.

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 have shown that the 4th International Standard is very stable in unopened ampoules stored at -20°C. The predicted loss of activity is <0.01% of the original potency per year for both Factors II and X when stored at -20°C.

Once reconstituted the activity of this preparation is assured for three hours when stored on melting ice.

9. REFERENCES

Campbell PJ. Procedures used for the production of biological standards and reference preparations. J Biol Standardisation. 1974, 2, 259-267.

10. ACKNOWLEDGEMENTS

We acknowledge all participants in the international collaborative study. We are grateful to BioProducts Laboratory Ltd, Grifols Biologicals Inc and Baxter AG for supply of candidate materials..

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

Physical and Chemical properties	
Physical appearance: White solid	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: Yes
Flammable: No	Handling: See caution, Section 2
Other (specify): Contains 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 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: ~25 mg
Toxicity Statement: Toxicity not assessed
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_biologicalstandardsrev2004.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.