Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

**Non WHO Reference Material**
**8th British Working Standard for Factors II, IX, X, Concentrate**
**NIBSC code: 23/284**
**Instructions for use**
**(Version 1.0, Dated 22/01/2025)**

This material is not for in vitro diagnostic use

## 1. INTENDED USE

The 8th British Working Standard for Blood Coagulation Factors II, IX, X, Concentrate, was established by the Medicines and Healthcare products Regulatory Agency in 2025. This standard consists of ampoules (coded 23/284) 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 collaborataive study involving 9 expert laboratories. Potencies were assigned against the 5th International Standard for Blood Coagulation Factor IX, 14/148, and the 4th International Standard for Blood Coagulation Factors II and X, Concentrate, 11/126. The assigned potencies after reconstitution with 0.5 ml distilled water are:

FII: 8.0 IU/ml, GCV 4.9%
FIX: 10.2 IU/ml, GCV 4.6%
FX: 8.0 IU/ml, GCV 5.6%

*GCV = Geometirc Coefficient of Variation

The uncertainty of measurement for 23/284, calculated as expanded uncertainty ranges corresponding to a 95% level of confidence (k=2.36 for FII and FX, k=2.31 for FIX) is calculated to be:

FII: 7.7-8.3 IU/ml
FIX: 9.9-10.6 IU/ml
FX: 7.7-8.4 IU/ml

## 4. CONTENTS

Country of origin of biological material: Italy.
The standard, 23/284, was prepared at the Medicines and Healthcare products Regulatory Agency in April 2024. The liquid bulk, prepared in 50 mM Tris, 150 mM NaCl, 2 mg/ml trehalose, 5 mg/ml human albumin, pH 7.4 buffer, was kept between 2-8 degrees C thoughout the distribution into approximately 23,000 ampoules.

## 5. STORAGE

Unopened ampoules should be stored in the dark at -20 degrees 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. 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 ampoule to equilibrate at room temperature for 10 minutes. Reconstitute the total contents with 0.5 ml distilled water using gentle agitation. Transfer the contents to a plastic tube. Assays should be carried out as soon as possible after reconstitution. It is not recommended to freeze-thaw aliquots after reconstution 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.

Accelerated degradation studies, using ampoules stored at elevated temperatures assayed relative to ampoules stored at -70 degrees C, have been initiated. Further data is required to make a prediction, however real-time degradation studies have shown that unopened ampoules stored at -20 degrees C do not show degradation after storage for 8 month when compared to the relevant International Standard.

On-bench stability assessments have shown that the material is stable for 3 hours when reconstituted and stored on melting ice in a plastic tube, however we recommend using the material as soon as possible after reconstitution

## 9. REFERENCES

Not applicable

## 10. ACKNOWLEDGEMENTS

We are grateful to the participants of the collaborative study and to Kedrion S.p.A and BioProducts Laboratories for donations of bulk 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

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

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 freeze-dried powder | Corrosive: No |
| Stable: Yes | Oxidising: No |
| Hygroscopic: Yes | Irritant: Unknown |
| Flammable: No | Handling: See caution, Section 2 |
| Other (specify): 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**

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|---|
| **Country of origin for customs purposes*:** United Kingdom<br>* 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:** 0.016 g |
| **Toxicity Statement:** Toxicity not assessed |
| **Veterinary certificate or other statement** if applicable.<br>**Attached:** No |

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
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