



**WHO International Standard
1st International Standard Factor XIII Plasma, Human
NIBSC code: 02/206
Instructions for use
(Version 7.0, Dated 02/12/2019)**

1. INTENDED USE

The WHO 1st International Standard for Blood Coagulation Factor XIII (FXIII) Plasma consists of ampoules, coded 02/206, containing aliquots of a freeze-dried human plasma containing FXIII. This preparation was established by the Expert Committee on Biological Standardization (ECBS) of the World Health Organization in November 2004¹.

This standard is intended to be used in the measurement of FXIII, both activity and antigen (A2B2 complex & Total FXIII-B subunit), in plasma and is primarily intended for calibration of secondary and/or in-house working FXIII plasma standards.

The latest ECBS report is available from the WHO (www.who.int/biologicals). Document number: WHO/BS/2019.2370².

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. The plasma for this preparation was prepared from pools of human plasma in which every donation was tested and found negative for hepatitis B surface antigen, antibodies to HIV-1 and -2 and antibodies to hepatitis C. The filled candidate preparation was subsequently 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 biological activity and antigen content (A2B2 complex) of the 1st International Standard for Blood Coagulation FXIII Plasma (coded 02/206), was calibrated in INTERNATIONAL UNITS (IU), in an international collaborative study involving 23 laboratories in 10 countries. This standard was additionally calibrated for Total FXIII-B subunit antigen in a further international collaborative study involving 7 laboratories in 6 countries

The assigned potencies are:

FXIII activity potency	- 0.91 IU per ampoule¹
FXIII A2B2 antigen potency	- 0.93 IU per ampoule¹
Total FXIII-B subunit antigen potency	- 0.98 IU per ampoule²

4. CONTENTS

Country of origin of biological material: United Kingdom.

The 1st International Standard for Blood Coagulation FXIII, Plasma (coded 02/206), contains freeze-dried (1 mL) aliquots of a pooled human plasma containing Factor XIII.

Frozen units of plasma were thawed and pooled. 1 molar solution of HEPES was slowly added and the pool gently stirred to give a final concentration of 0.04M HEPES. The pooled buffered plasma was then distributed at 4°C into ampoules, coded 02/206 and the contents of the ampoules were freeze-dried under the conditions normally used for international biological standards³.

5. STORAGE

Unopened ampoules should be stored at -20°C. After reconstitution, any unused material must be discarded, not frozen for later use.

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. The total contents of the ampoule should be reconstituted at room temperature with 1 ml distilled water, dissolved by gentle swirling to avoid froth and transferred immediately to a suitable plastic tube. The reconstituted Standard is stable for up to 2 hours at room temperature.

N.B. If using this Standard to calibrate Factor XIII concentrates, the test concentrates MUST be pre-diluted in FXIII deficient plasma, before making the assay dilutions. Assay dilution buffers should contain 1% albumin, preferably clinical grade.

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.

Accelerated degradation studies have shown that this standard is extremely stable both when stored at -20°C and at mailing temperatures. Predicted loss of both FXIII activity & FXIII antigen (A2B2 complex) when stored at -20°C were below 0.05% per year. Real-time stability studies, after 17 years storage at -20°C, has shown no loss in FXIII-B subunit antigen potency.

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

9. REFERENCES

1. Raut S, Merton RE, Rigsby P, Muszbek L, Seitz R, Ariens RA, Barrowcliffe TW, Ichinose A; ISTH/SSC Factor XIII Subcommittee and the Factor XIII Standardization Working Party. A collaborative study to establish the 1st International Standard for factor XIII plasma. J Thromb Haemost. 2007; 5(9): 1923-9.

2. Raut S, Katona É, Coxon C, Riches-Duit A, Muszbek L, Schroeder V, Rigsby P. A collaborative study to additionally assign value for total factor XIII-B subunit antigen to the WHO 1st International Standard for Factor XIII Plasma, (02/206). WHO ECBS Report: BS.2019.2370. 2019.

[https://www.who.int/biologicals/expert_committee/BS.2019.2370_AdditionalAssign_Value_for_Total_Factor_XIII-B_Subunit_Antigen_to_the_WHO_1st_IS_for_Factor_XIII_Plasma_\(02-206\)_FINAL.pdf](https://www.who.int/biologicals/expert_committee/BS.2019.2370_AdditionalAssign_Value_for_Total_Factor_XIII-B_Subunit_Antigen_to_the_WHO_1st_IS_for_Factor_XIII_Plasma_(02-206)_FINAL.pdf)



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

10. ACKNOWLEDGEMENTS

Are made to all the participants in the study and to the North London Blood Transfusion Centre for supplies of the candidate material for the study. We would also like to express our sincere thanks to ISTH/SSC FXIII & Fibrinogen Subcommittee and to the ISTH/SSC FXIII Standardisation Working Party (SWP) for their guidance.

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: Freeze dried powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
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: 0.09g
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 and other biological reference standards 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.