Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
2nd International Standard for Factor XIII Plasma, Human
NIBSC code: 20/292
Instructions for use
(Version 1.0, Dated 30/01/2023)

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1. INTENDED USE

The WHO 2nd International Standard for Blood Coagulation Factor XIII (FXIII) Plasma consists of ampoules, coded 20/292, 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 October 2022 (1).

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 callibration of secondary and/or in-house working FXIII plasma standards.

The latest ECBS report is available from the WHO (www.who.int/). Document number: WHO/BS/2022.2437 (1).

2. CAUTION

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. This preparation is not for administration to humans or animals

3. UNITAGE

The biological activity and antigen content (A2B2 complex & Total FXIII-B subunit) of the 2nd International Standard for Blood Coagulation FXIII Plasma (coded 20/292), was calibrated in INTERNATIONAL UNITS (IU), in an international collaborative study involving 13 laboratories in 7 countries.

The assigned potencies are:

FXIII activity potency - 1.04 IU per ampoule (1)

FXIII A2B2 antigen potency - 0.98 IU per ampoule (1)

Total FXIII-B subunit antigen potency - 0.92 IU per ampoule (1)

4. CONTENTS

Country of origin of biological material: United Kingdom.
The 2nd International Standard for Blood Coagulation FXIII, Plasma (coded 20/292), 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 20/292 and the contents of the ampoules were freeze-dried under the conditions normally used for international biological standards (2).

5. STORAGE

Unopened ampoules should be stored at -20ºC. 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.
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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.

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

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 when stored at -20°C was 0.001% per year.

9. REFERENCES

1. Riches-Duit A, Katona É , Cherrington S, Muszbek L, Atkinson E, Rigsby P, Raut S. Proposed WHO 2nd International Standard for Factor XIII, Plasma (20/292). WHO ECBS Report: BS.2022.2438
2. 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 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:

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

World Health Organization

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_biolefstandardsrev2004.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.