Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
1st INTERNATIONAL STANDARD FOR FIBRINOGEN CONCENTRATE
NIBSC code: 98/614
Instructions for use
(Version 4.0, Dated 01/04/2008)

1. INTENDED USE

The 1st International Standard for Fibrinogen Concentrate, consists of ampoules, coded 98/614, containing aliquots of a freeze-dried concentrate of fibrinogen prepared from human plasma. This preparation was established as the 1st International Standard for Fibrinogen concentrate by the Expert Committee on Biological Standardisation of the World Health Organisation in 2000, with labelled contents of total protein and clottable protein. (WHO/BS/00.1927 - document available from WHO).

This standard is intended to be used in the measurement of fibrinogen in concentrates and is primarily intended for calibration of secondary and/or in-house working standards of fibrinogen 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 17 laboratories in an international collaborative study in 7 countries. Total protein was measured by three methods; absorbance at 280nm, dye binding (including biuret), and protein nitrogen (kjeldahl). Clottable protein was measured by the same methods after dissolution of the clot; two additional methods were – absorbance (280nm) as the supernatant after clot removal, and the Clauss method.
The assigned potencies are:

Total Protein - 15 mg per ampoule
Clottable Protein - 10.4 mg per ampoule

4. CONTENTS

Country of origin of biological material: United Kingdom.
The 1st International Standard for Fibrinogen Concentrate (coded 98/614), contains freeze-dried (1 mL) aliquots of a pooled concentrate containing Fibrinogen.

A frozen bulk preparation of fibrinogen concentrate was thawed and diluted to a concentration of approximately 15mg/ml total protein in a buffer of 20mM Tris, 40mM tri-sodium citrate and 3% (w/v) sucrose, pH 7.25. The solution was filtered and filled at 4ºC into approximately 4,000 ampoules coded 98/614 (with an inter-ampoule cv of 0.11%) and the contents of the ampoules were freeze-dried under the conditions normally used for international biological standards[1]. After freeze-drying and secondary desiccation, the average residual moisture was 0.13%.

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.

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.

The International Standard is intended for calibration of internal house standards of fibrinogen concentrate used as therapeutic materials either alone or as part of fibrin sealant kits. It is suggested that, whichever assay is used, values for the house standard are expressed as a percentage of the International Standard, then multiplied by the appropriate assigned value of total or clottable protein in the International Standard. For absorbance and Clauss assays it is recommended that several dilutions of both International and house standards are tested.

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 the standard is extremely stable. No detectable losses of total protein or clottable protein were found in ampoules stored for up to 19 months at 45ºC.

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

9. REFERENCES

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

10. ACKNOWLEDGEMENTS

The contributions of all the participants in the study are gratefully acknowledged. We are grateful to donors for the supply of concentrates for the study.

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

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

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: Unknown
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: 0.06g
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.

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