Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Working Standard
14th BRITISH STANDARD FOR COAGULATION FACTOR VIII CONCENTRATE, HUMAN
NIBSC code: 17/206
Instructions for use
(Version 1.0, Dated 21/05/2018)

This material is not for in vitro diagnostic use.

1. INTENDED USE

The 14th British Standard for Blood Coagulation Factor VIII Concentrate, Human, consists of glass ampoules (code labelled 17/206) containing 1ml aliquots of human Factor VIII concentrate, freeze-dried. A potency of 9.5 INTERNATIONAL UNITS FVIII:C PER AMPOULE has been assigned. This standard has been calibrated for Factor VIII coagulant activity (FVIII:C) using only the chromogenic method. This standard is primarily intended to be used as a secondary working standard for estimation of FVIII:C potency in plasma derived FVIII concentrates, using chromogenic assays.

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 14th British Standard was calibrated by assay relative to the WHO 8th International Standard Factor VIII Concentrate (07/350) in a collaborative study involving four laboratories, where value assignment for FVIII:C was carried out only using the chromogenic method. Estimates relative to WHO 8th International Standard gave an assigned FVIII potency value of:

9.5 International Units per ampoule.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The 14th British Standard was prepared in November 2017 using a plasma-derived high purity Factor VIII Concentrate. All donations used to prepare this product were tested and found negative for HBsAg, anti-HIV-1 and -2, anti-HCV, HCV-RNA (plasma pools). Manufacturing of this product also included 2 viral inactivation steps, solvent/detergent and terminal heat treatment at 80°C for 72 hours, which inactivate both non-enveloped and enveloped viruses. After reconstitution of the product, the concentrate material was pooled and formulated in the following buffer: 0.1M NaCl, 10mM Tris-HCl (pH 7.5) 1mM Calcium Chloride, 1mg/ml Trehalose, 2mg/ml human albumin. The formulated material was filled and freeze-dried in sealed glass ampoules at NIBSC, under conditions required for International Standards[1]. One mL of this material was dispensed into each of approximately 18,000 ampoules. The mean filling weight was 1.0084g with the coefficient of variation (CV) of 0.14% based on 617 check-weight samples. Mean residual moisture after freeze-drying was 0.39% (CV 17.3%, n=12) and mean oxygen headspace was 0.25% (CV 39.1%, n=12).

5. STORAGE

Store unopened ampoules in the dark at -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 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
Reconstitute the total contents of each ampoule after warming to room temperature, with 1.0 ml of distilled water, using gentle shaking. Transfer the solution to a plastic tube and keep at room temperature during the assay. Fresh ampoules of standard should be used for each assay.

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.

Stability has been assessed in an accelerated degradation study. A predicted degradation rate of 0.016% per year has been obtained for ampoules stored at -20ºC. The standard must only be used with the assigned potency and users should not adjust the assigned potency on the basis of this prediction.

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

9. REFERENCES

1 Campbell PJ. Procedures used for the production of biological standards and reference preparations. J Biol Standardisation, 1974; 2: 259- 67.

10. ACKNOWLEDGEMENTS

We are grateful to the Bio Products Laboratory, Elstree, UK for the supply of FVIII concentrate used in the production of this standard and to the staff of Standards Processing Division (NIBSC) for ampoule filling, freeze-drying and processing the candidate & trial preparations and for the dispatch of collaborative study samples to participants. The participation of Kedrion Biopharmaceuticals S.p.A, Lucca, Italy and Bio Products Laboratory, Elstree, UK in the calibration exercise is gratefully acknowledged.

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.

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WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

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: Solid		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: 0.02g
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable**.** **Attached:** No