Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
9th International Standard Factor VIII Concentrate, Human
NIBSC code: 21/142
Instructions for use
(Version 1.0, Dated 12/07/2023)

This material is not for in vitro diagnostic use

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.

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

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 WHO 9th International Standard was calibrated in INTERNATIONAL UNITS (IU) in an international collaborative study involving 26 laboratories in 12 countries. A potency of

9.5 INTERNATIONAL UNITS (IU) per ampoule

has been assigned. This figure is based on comparison with the 8th International Standard for Factor VIII Concentrate, using one-stage and chromogenic assays.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The WHO 9th International Standard for Blood Coagulation Factor VIII:C, Concentrate, consists of a freeze-dried plasma-derived FVIII concentrate formulation with clinical grade human albumin.
The concentrate freeze-dried material was reconstituted in sterile distilled water and diluted to a final volume of approximately 20 litres in a buffer containing: 50 mM Sodium Chloride, 267 mM Glycine (pH 7.3), 18.7 mM Tri-Sodium Citrate.2H2O, 10 mg/ml human albumin and other proprietary excipients. It was then distributed at 4 degrees Celsius into glass ampoules, coded 21/142 and the contents of the ampoules were freeze-dried under the conditions normally used for international biological standards (2). The mean content of 704 ampoules before freeze-drying was 1.0079 g (range 1.0030 g to 1.0140 g) and the coefficient of variation was 0.20%. Estimnates of residual moisture after freeze-drying have a mean value of 0.58% (n=12). Estimates of oxygen in the headspace gave a mean value of 0.08% (n=12).

5. STORAGE

Unopened ampoules should be stored at -20 degrees 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 platic tube. The reconstituted Standard is stable for up to 3 hours when kept on melting ice.
N.B. when using this Standard to calibrate other concentrates, both standard and test concentrate MUST be pre-diluted in FVIII-deficient plasma, either haemophilic plasma, or artificially depleted plasma containing normal levels of VWF, 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 stable both when stored at -20 degrees C and at mailing temperatures.
Predicted loss of FVIII:C when stored at -20 degrees C could not be predicted as there was insufficient loss in potency after 12 months storage at elevated degradation temperatures.
NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

(1) Sanj Raut, Andrew Riches-Duit, Sophie Cherrington, Eleanor Atkinson, Paul Matejtschuk and Peter Rigsby. Proposed WHO 9th Internation Standard for Blood Coagulation Factor FVIII Concentrate (21/142). WHO ECBS Report BS/2023.2444.
(2) Campbell PJ. Procedures used for the production of biologicial standards and reference prepatations. J Biol Standardization, 1974, 2: 259-267.

10. ACKNOWLEDGEMENTS

We would like to acknowledge all the participants in the study. We would also like to express our thanks to CSL Behring GmbH (Germany), Grifols SA (Spain) and Octapharma AB (Sweden/France) for their kind donations of materials 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

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

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: 0.09 g
Toxicity Statement: Toxicity not assessed
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.