Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
2nd INTERNATIONAL STANDARD FACTOR VIIa CONCENTRATE
NIBSC code: 07/228
Instructions for use
(Version 4.0, Dated 30/11/2012)

1. INTENDED USE

The 2nd International Standard for Factor VIIa, concentrate, was established by the Expert Committee on Biological Standardization of the World Health Organization in October 2008. The preparation consists of ampoules (coded 07/228) containing 1ml aliquots of Factor VIIa concentrate, freeze-dried. Details of the collaborative study can be found in document WHO/BS/08.2090. The standard is primarily intended for the relative potency estimation of therapeutic concentrates of activated factor VII.

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 potency of the standard was determined by one-stage clotting assay against the 1st IS Factor VIIa Concentrate (89/688), in an international collaborative study involving 23 laboratories in 12 countries. The overall mean potency assigned to each ampoule of the 2nd IS is 656 IU.

Uncertainty: the International Unit of 07/228 is assigned without uncertainty. Where required, the uncertainty of the ampoule content of 07/228 may be considered to be the co-efficient of variation of the fill volume, which was determined to be 0.17 %.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The International Standard was prepared at the National Institute for Biological Standards and Control in November 2008.
The liquid Factor VIIa concentrate formulation was kept at 2 - 8 °C throughout distribution into 10,000 ampoules, then freeze-dried under conditions used for international biological standards (1). The mean liquid filling weight was 1.0050g (range 1.0010 - 1.0100 g) with a coefficient of variation of 0.17%.

5. STORAGE

Unopened ampoules should be stored in the dark at -20 °C or below.
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 of the standard at room temperature with 1.0ml distilled water using gentle shaking. Transfer the solution to a plastic tube. Assays should be carried out as soon as possible after reconstitution. Studies have shown that the reconstituted standard is stable for 4 hours when stored in a plastic tube on melting ice. It is not recommended to freeze aliquots after reconstitution for subsequent use.

8. STABILITY

Reference materials are held at NIBSC within assured temperature-controlled storage facilities and they should be stored on receipt as indicated on the label. It is the policy of WHO not to assign an expiry date to their international reference materials. Accelerated degradation studies have indicated that this material is suitably stable, when stored at -20 °C or below, for the assigned values to remain valid until the material is withdrawn or replaced. These studies have also shown that the material is suitably stable for shipment at ambient temperature without any effect on the assigned values. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES

1. Campbell P. J. Procedures used for the production of biological standards and reference preparations. Journal of Biological Standardization (1974) 2, 259-267

10. ACKNOWLEDGEMENTS

We are very grateful to Novo Nordisk A/S, Denmark and to the Chemo-Sero-Therapeutic Research Institute, Kumamoto, Japan for supplying the candidate materials and to the participants in the collaborative 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

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

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

World Health Organization

Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	
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: 0.030 g
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.