Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
5th International Standard for Blood Coagulation Factor IX, Concentrate
NIBSC code: 14/148
Instructions for use
(Version 1.0, Dated 19/11/2015)

1. INTENDED USE

The 5th International Standard for Blood Coagulation Factor IX, Concentrate Human was established by the Expert Committee on Biological Standardisation of the WHO in October 2015. This batch of standard, consists of ampoules (coded 14/148) containing aliquots of freeze-dried blood coagulation factor IX, concentrate, is intended for the calibration of factor IX functional activity in theraputic 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 potency of the standard was determined by one-stage clotting and chormogenic assays in 49 laboratories from 18 countries against the 4th International Standard for FIX, Concentrate (07/182). The overall mean potency assigned is 10.5 IU/ampoule. The detail of the collaborative study is described in WHO/BS/2015.2261 and is available from the WHO (http://www.who.int/biologicals/expert_committee/BS2261_Establishment_Factor_IX_5th_WHO_IS.pdf).

Uncertainty: As a WHO international standard, there is no certainty associated with the assigned value of 14/148. Where required, the certainty of the ampoule content is taken as the coefficient of variation of the fill which is estimated to be 0.24%.

4. CONTENTS

Country of origin of biological material: United Kingdom.
The standard, 14/148 was prepared at the National Institute for Biological Standards and Control in June 2014. The liquid bulk in 50mM TRIS, 150mM NaCl, 2mg/ml Trehalose, 10mg/ml human albumin, pH 7.4 buffer, was kept between 2 - 8°C throughout the distibution into ampoules. The mean liquid fill weight was 1.0086, with a coefficient of variation of 0.24%.

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

Allow the ampoule to equibrate at room temperature for 10 minutes. Reconstitute the total content with 1.0 ml distilled or deionised water using gentle agitation. Transfer the content to a plastic tube. Assays should be carried out as soon as possible upon reconstitution. A study in one laboratory has shown that the reconstitued material was stable up to 4 hours when stored on melting ice. It is not recommended to freeze thaw aliquots after reconstitution for subsequent use.

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. It is the policy of WHO not to assign expiry dates to international reference materials. They remain valid with the assigned potency and status until withdrawn or amended.

The stability of this standard has been assesseed in an accelerated degradation study which involved potency estimation of ampoules stored at elevated temperatures relative to ampoules stored at -150°C. Estimation of predicted loss has indicated no loss of activty when stored at -20°C, and at +20°C less that 0.7% activity per year which supports the shipment of this standard at ambient temperature. The accelerated degradation study and real time monitoring will continue for the lifetime of the standard.

9. REFERENCES

N/A

10. ACKNOWLEDGEMENTS

We are grateful to the participants of the collaborative study, Wyeth BioPharma, USA; CSL Behring, USA; Emergent Biosolutions, Canada and Baxter BioScience AG, Austria for the kind donation of candidate materials and the support of the FVIII/FIX subcommittee of the Scientific and Standardisation Committee (SSC) of the Interantional Society on Thrombosis and Haemostasis (ISTH)

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: White freeze-dried powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	Yes	Irritant:	Unknown
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	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: 0.0316g
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.