



**WHO International Standard
2nd International Standard for FIXa
NIBSC code: 14/316
Instructions for use
(Version 1.0, Dated 29/11/2017)**

1. INTENDED USE

The 2nd International Standard for Activated Factor IX (FIXa), Human, coded 14/316 consists of ampoules containing aliquots of a freeze-dried purified human FIXa prepared from activated recombinant human Factor IX. This preparation was established as the 2nd International Standard for Activated Factor IX, Human, by the Expert Committee on Biological Standardisation of the World Health Organisation in October 2017. The intended use of this standard is for measurement of FIXa. The ECBS report is available at http://www.who.int/biologicals/expert_committee/BS2325_FIXa.pdf?ua=1

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 2nd International Standard for FIXa was calibrated by 19 laboratories from 9 different countries against the 1st International Standard for FIXa, 97/562 by purified reagent functional activity methods specific for FIXa. The assigned potency of this preparation is

10.5 IU/ampoule.

The unit of FIXa as defined by this standard is not identical to a unit of purified Factor IX when fully activated.

4. CONTENTS

Country of origin of biological material: USA.

The bulk starting material for 14/316 was prepared by FXIa activation of human recombinant FIX. The purity of the FIXa was assessed and confirmed by PAGE with silver staining. The estimated specific activity of the bulk was 612 IU/mg. Sixty-two ml of the frozen bulk was thawed at 37°C diluted in buffer (0.05M Tris, 0.15M NaCl, 5 mg/ml trehalose, 1.25% human albumin, pH 7.4) to approximately 10 IU/ml. The solution was distributed into approximately 18,000 ampoules at 4°C and freeze-dried. The mean weight of the liquid content 1.0083g (n = 410). As a WHO International Standard, there is no uncertainty associated with the assigned value of 14/316. Where required the uncertainty of the ampoule content is taken as the coefficient of variation of the fill which has been estimated to be 0.169%.

5. STORAGE

Unopened ampoules should be stored in the dark at or below -20°C. Allow ampoules to warm to room temperature before opening and reconstitution.

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

Open ampoule, taking care to ensure that all material is in the lower part and reconstitute with 1.0 ml of distilled water. The reconstituted Standard should be used as soon as possible. On-bench stability study in one laboratory suggests the reconstituted standard would be stable up to 4 hours when stored on melting ice.

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 an expiry date to their international reference materials. They remain valid with the assigned potency and status until withdrawn or amended.

Accelerated degradation studies, which involves potency estimation of ampoules stored at elevated temperatures relative to ampoules stored at below -150°C, of 14/316 showed no predicted loss of FIXa activity when the preparation is stored at -20°C or below. The predicted loss for the Standard stored at +20°C was 0.01% per year and this supports shipment 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

Pfizer Inc (Andover, Massachusetts, USA) for kind donation of the bulk FIXa. The participants of the international 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.

based on the report of the international collaborative study which established their suitability for the intended use.

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 solid	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: Yes
Flammable: No	Handling: See caution, Section 2
Other (specify):	contains recombinant and human plasma derived material
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: 0.03g
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_bi_olestandardsrev2004.pdf (revised 2004). They are officially endorsed by the WHO Expert Committee on Biological Standardization (ECBS)