Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
2nd International Standard for High Molecular Weight Urokinase
NIBSC code: 11/184
Instructions for use
(Version 2.0, Dated 24/01/2013)

1. INTENDED USE

The potency of the Standard was determined by International Collaborative Study and found to be 3200 IU per ampoule in comparison with the 1st International Standard for High Molecular Weight Urokinase (87/594) (1). The Standard was established by the Expert Committee on Biological Standardisation of the World Health Organisation (WHO) in October 2012 and full details of the calibration study can be found in document WHO/BS/2012.2205. The potency of 3200 IU per ampoule was assigned using fibrin-based clot lysis assay methods. Caution is advised when interpreting results using alternative assay methods. This Standard is intended for use as an activity standard in enzymatic assays. Active site titration of the bulk material provided an estimate for active enzyme in the ampoule, after reconstitution with 1 ml water, of 380 nM, equivalent to approximately 21 µg urokinase per ampoule. However this value is only an estimate from one laboratory and should be treated as a guide only. The Standard has not been assigned a value for antigen.

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

3200 IU/ampoule.

4. CONTENTS

Country of origin of biological material: United Kingdom, Italy.

5. STORAGE

Unopened ampoules should be stored in the dark at or below -20ºC
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
Each ampoule contains the residue after freeze drying of 1ml solution of 10mM Hepes buffer, pH7.4, containing 0.15 M NaCl and 5 mg human albumin This solution was filled into approximately 4700 ampoules with mean fill weight of 1.0099 g and inter-ampoule CV of 0.14%. After freeze drying the average residual moisture was 0.4%. Before opening, ampoules should be allowed to come to ambient temperature and the contents dissolved by addition of 1 ml of distilled water.

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. 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

Campbell PJ. Procedures used for the production of biological standards and reference preparations. Journal of Biological Standardisation (1974) 2, 259-267.

10. ACKNOWLEDGEMENTS

Participation of all laboratories in the International Collaborative Study to establish the potency of the 2rd International Standard for High Molecular Weight Urokinase, 11/184, is gratefully acknowledged (see WHO/BS/2012.2205 for full details). We also acknowledge the help of the SSC/ISTH sub-committee on Fibrinolysis and the Standards Processing Division of NIBSC.

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): 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: *20 mg*
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.