Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
WHO 3rd IS for Tissue Plasminogen Activator, Human, recombinant
NIBSC code: 98/714
Instructions for use
(Version 3.0, Dated 26/03/2008)

1. INTENDED USE

The potency of the Standard was determined by International Collaborative Study and found to be 10000 IU per ampoule (1) in comparison with the 2nd International Standard for tissue plasminogen activator (86/670), which is from melanoma cell culture (2). The Standard was established by the Expert Committee on Biological Standardisation of the World Health Organisation (WHO) in October 2000. Results from the International Collaborative Study suggest that the 3rd International Standard for tissue plasminogen activator (98/714) is a suitable standard for the melanoma cell-derived enzyme and the recombinant enzyme, and may be suitable for assaying tissue plasminogen activator from other sources (1). The potency of 10000 IU per ampoule for the 3rd International Standard for tissue plasminogen activator (98/714) was assigned using fibrin-based 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. The Standard has not been calibrated as an antigen standard.

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

10000 IU/ampoule

4. CONTENTS

Country of origin of biological material: United Kingdom.

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

Tissue Plasminogen Activator (EC 3.4.21.68), also known as Plasminogen Activator, Tissue type and commonly abbreviated to tPA (or t-PA) is a serine protease that activates plasminogn to plasmin. This Standard was prepared using commercial, therapeutic, recombinant, tissue plasminogen activator (Alteplase), expressed and purified from CHO cell culture in a predominantly single chain form. Each ampoule contains the residue after freeze drying of 1ml solution of 60mM sodium phosphate buffer, pH7.4, containing 5 mg human albumin and approximately 20 microgram tissue plasminogen activator. This solution was filled into approximately 4000 ampoules with an inter-ampoule cv of 0.09%. After freeze drying and secondary desiccation , the average residual moisture was 1.0%.

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.

Assays were performed on samples of 98/714 stored at elevated temperatures for 0.5 years and were repeated after 1.2 years. Analysis of the pooled data from all temperatures indicated the most pessimistic estimate for the upper limit for the 95% confidence interval of activity loss at -20ºC was only 0.26% per year (with a mean predicted loss of 0.037% per year).

9. REFERENCES

1) Dawn Sands, Colin M. Whitton, R. Elizabeth Merton, Colin Longstaff. A collaborative study to establish the 3rd International Standard for tissue plasminogen activator. Thromb. Haemost. 88: 294-7 (2002).

2) Patrick J Gaffney, Antony D Curtis. A collaborative study to establish the 2nd International Standard for tissue plasminogen activator (t-PA). Thromb. Haemost. 58: 1085-7 (1987)

10. ACKNOWLEDGEMENTS

Participation of the following laboratories in the International Collaborative Study to establish the potency of the 3rd International Standard for tissue plasminogen activator (98/714) is gratefully acknowledged.

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

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

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: *10 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.