Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
International Standard for Plasminogen Activator Inhibitor-1 (PAI-1) Plasma, Human
NIBSC code: 92/654
Instructions for use
(Version 3.0, Dated 02/04/2008)

1. INTENDED USE

The Standard consists of reactivated recombinant (in Chinese hamster ovary cells) PAI-1 (1) added to normal human plasma and lyophilized following ampouling at NIBSC.

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 Standard for PAI-1 was calibrated in terms of neutralisation of the two major plasminogen activators, tissue-type plasminogen activator (t-PA) and urinary-type plasminogen activator (u-PA) in an international collaborative study (2) involving 8 laboratories. The standard was found to contain:

27.5 IU (t-PA neutralisation)
7.0 IU (u-PA neutralization)

The international standards for t-PA (3) and u-PA (4) were used by the participants to establish this dual unitage of the PAI-1 standard. The standard was established by WHO at the 46th meeting of its Expert Committee on Biological Standardization in October 1995.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Nine 500 ml packs of fresh frozen single donor human plasma were received from the North London Blood Transfusion Centre (Colindale, London). All single donor plasmas were tested and found negative for HIV antibodies and hepatitis B surface antigen and HCV antibody. Antigen PAI-1 analysis performed by Professor Paul Declerck (University of Leuven, Belgium) indicated that two of the single donations contained > 40 mgs of PAI-1 antigen and these were discarded. The other 7 plasma packs were mixed giving rise to 3,500 mls of plasma. To this plasma was added reactivated recombinant (CHO cell) PAI-1 (kindly donated by Professor Paul Declerck) at a presumed level of approximately 250 ngs per ml of plasma. This PAI-1 has been reactivated with acid which results in the formation of 10-15% active PAI-1 from the original recombinant antigen (1). Data from this study indicated each ampoule of the standard to contain 10-12 mole of active PAI-1.

These data on antigen concentration of the recombinant PAI-1 were supplied by Professor Paul Declerck and were based on amino-acid analysis data. The PAI-1 enriched plasma was distributed into neutral glass ampoules (1ml) coded 92/654 and the procedures for freeze drying and ampouling described by Campbell (5) were followed with the exception that secondary desiccation was for 3 days.

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

Allow ampoules to warm to room temperature. Open ampoule, taking care to ensure that all material is in the lower part, and reconstitute with 1.0ml 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.

9. REFERENCES

1. Declerck P.J. et al (1988) Purification and characterization of natural and recombinant human plasminogen activator inhibtor-1 (PAI-1). Eur J Bioch 175, 531-540

2. Gaffney P.J., Edgell T. A., (1996) An international standard for plasminogen activator inhibitor-1 (PAI-1). Thromb Haemost (submitted).

3. Gaffney P.J., Curtis A.D., (1987) A collaborative study to establish the 2nd International Standard for tissue plasminogen activator (t-PA), Thromb Haemost 58, 1085-1087.

4. Gaffney P.J., Heath A.B., (1990) A collaborative study to establish a standard for high molecular weight urinary-type plasminogen activator (HMW/u-PA). Thromb Haemost 64, 398-401.

5. Campbell P.J., (1974) International biological standards and reference materials. I. Preparation and presentation of materials to serve as standards and reference preparations. J Biol Stand 2, 249-258.

10. ACKNOWLEDGEMENTS

Participating laboratories in the collaboration study are greatfully 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

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: Freeze dried powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: Unknown
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: *50 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.

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